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THE INNERVATION OF STRIATED MUSCLE.

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Introduction.

SINCE the publication in 1909 of Boeke's work on the sympathetic innervation of striated muscle a great amount of work has been done to try to verify or to disprove his hypothesis, but in spite of the rather intensive activity, the subject is still a matter of dispute.

Boeke[1]-[5] has demonstrated the presence of fine endings which he states are sympathetic in origin, and which are claimed to represent the mechanism by means of which the tone of muscle is maintained. According to Boeke's hypothesis, then, striated muscle fibres are supplied not only by cerebro-spinal nerves (somatic nerves), but also by sympathetic nerves.

Hunter,[6][7] however, who became interested in Royle's work on the problem of spastic paralysis, conceived the idea based on Kulchitsky's[8] observations on reptilian muscle tissue, that one set of muscle fibres is innervated by somatic nerves and another set by sympathetic nerves and he and Latham[10] produced what they claimed was evidence in support of this view.

When Hunter was in London in 1922, he saw Kulchitsky's preparations of python muscle, showing the two types of endings, namely, (i) the plate-like called *"terminaisons en plaque"* which were considered to be of undoubted cerebro-spinal origin, that is, somatic, and (ii) the grape-like endings, called *"terminaisons en grappes"* which Kulchitsky stated were probably sympathetic. As these two types of ending had not been observed by Kulchitsky to end in relation to the same muscle fibre, Hunter concluded that one group of muscle fibres was supplied by somatic and another by sympathetic nerves. He seemed to get further proof of this hypothesis when he and Latham examined preparations from the extrinsic eye muscles of the goat and discovered sprays of grape-like endings in relation to the muscle fibres.

This was the stage reached by Hunter in the investigation when the present writer took it up in the same laboratory. Accordingly, with the object of trying to throw further light on this interesting problem and particularly to seek evidence in support of Hunter's hypothesis, a general and extensive survey was made of the innervation of the striated muscle from representatives of the principal tetrapod groups, namely, amphibia (frog and salamander), reptilia (lizard and python) and mammals (echidna, bandicoot, kangaroo, rabbit, goat, horse, mouse, guinea-pig, monkey and man).

The main part of the work was carried out in the Department of Anatomy at the University of Sydney and this article was originally submitted for publication in November, 1928. Since then, however, I have had the privilege as a Fellow of the Rockefeller Foundation, of spending some months at the laboratories of Professor Boeke, in Utrecht, Holland, and of Professor Agduhr, in Upsala, Sweden, and through the courtesy of these investigators have seen at first hand the actual preparations which represent the principal evidence in support of the sympathetic innervation of striated muscle fibres. I also met and discussed these problems with Professor Woollard in Adelaide and with Professor Bielschowsky in Berlin. The latter gave me the opportunity of studying some very beautiful preparations of muscle made according to his own technique. As the printer's proofs of this article have been sent to me for correction from Australia, this has afforded me the opportunity of amending it so as to add my impressions of the evidence put forward in support of the sympathetic innervation of striated muscle fibres, based on a careful examination of the original preparations.

Technique.

The tissues were stained by the *intra vitam* methylene blue method of Ehrlich as described by Wilson[11] and by the gold chloride method of Ranvier as described by Garven,[12] with modifications in each case. The most important modification in the gold chloride technique and that which contributed so largely towards the brilliancy of the specimens obtained, consisted of thoroughly washing out the piece of tissue to be stained by means of saline solution, slightly hypotonic for the animal concerned. The clearing away of all blood elements enables the nerves on blood-vessels to be traced more readily and avoids the formation of deposits which are likely to be confused with nerve endings.

With regard to the cutting and mounting of the tissue after staining, a method was devised which enabled specimens to be obtained which gave more reliable evidence of the origin and destination of the nerve fibres. From the drawings which accompany some of the earlier works, it appears that some of the specimens were overteased and needlessly distorted. To overcome this difficulty the teasing of specimens was reduced to a minimum and a method of cutting and pressing devised. This consists of cutting out small pieces of muscle and separating them parallel to their long axes and then pressing them out on a slide under the cover-slip by means of a rod covered at the end by a piece of rubber tubing.

"Terminaisons en Grappes."

In the light of observations made by Kulchitsky, Hunter and Latham, a search was first made for the grape-like endings and as so much interest has centred around the occurrence and significance of this type of ending, it is proposed to discuss this subject first.

Very successful preparations were made both by the methylene blue and by the gold techniques and although the *terminaisons en grappes* were found

to occur constantly in all the muscles of the lower cold-blooded vertebrates, for example, the frog, salamander, lizard and python, yet in mammals they were observed only in the extrinsic eye muscles and in tongue muscles.

In addition to this limitation of their area of distribution, however, the *terminaisons en grappes*, seen in mammalian muscle tissue, presented different relations with the muscle fibres from those seen in amphibians and reptiles.

In mammals the *terminaisons en grappes* were always seen to be external to the sarcolemma of the muscle fibres, that is epilemmal, and occurred only among muscle fibres all of which could be made out to have an ordinary hypolemmal (motor) *terminaison en plaque*. In mammals, therefore, *terminaisons en grappes* are for this reason considered to be the endings of afferent or sensory nerve fibres.

In amphibians and reptiles, on the other hand, many of the *terminaisons en grappes* were seen to be definitely hypolemmal and are to be regarded, therefore, as endings of efferent or motor nerve fibres. Ordinary plate-like endings, however, were seen in these cold blooded animals, but it was noticed that they occurred only on the larger muscle fibres, while the hypolemmal *terminaisons en grappes* were seen only on the relatively smaller muscle fibres. Moreover, it was observed that individual muscle fibres received only the one type of nerve ending. It therefore appeared quite evident that some of the *terminaisons en grappes* seen in amphibian and reptilian muscle tissue were radically different from those seen in mammals and also that *terminaisons en grappes* could not be regarded as a definite functional type of nerve ending.

Further, it was also observed that in young mammals and in some muscles of certain older mammals the motor plates often simulated the grape-like endings in that the terminal twigs of the axonal expansions in the sole plates often ended in grape-like or beaded shaped structures rather than in the fucoid or seaweed shaped fronds usually described and as shown in Figures III, XXII and XXX. The significance of this will be discussed below.

From these general remarks, based on a survey of a wide field of observations, we will pass to a more detailed and particular account of the *terminaisons en grappes* as seen in the present investigation.

"Terminaisons en Grappes" in Striated Muscle of the Lizard.

The most significant observations on these grape-like terminations were made on preparations of lizard muscle; these will therefore be described first. The lizards whose tissue was used in this investigation, were mainly the blue tongue lizards (*Tiliqua scincoides*). One of the first important observations made on examining these preparations was that some of the *terminaisons en grappes* appeared to come off medullated nerves. To confirm this observation, a lizard's muscle was stained *intra vitam* with methylene blue and subsequently fixed in a saturated solution of ammonium molybdate to which had been added osmic asid as suggested by Wilson. By this technique the axis cylinders are stained blue and the myelin sheath a smoky colour. It was soon demonstrated by this method that many of the *terminaisons en grappes* came off medullated nerves. Sometimes the small bundles of fibres going to a group of terminations were noticed to be composed of fibres which were myelinated almost up to the endings and sometimes no sheath could be detected at all. If, however, these non-medullated fibres were traced back, they were found to emerge from a bundle of medullated ones and if they were further traced along this bundle, they could be observed to come off from a medullated fibre at a node of Ranvier. Once it was definitely shown by the methylene blue technique that these *terminaisons en grappes* arose from medullated nerves, the gold-stained preparations were carefully looked over for the evidence as disclosed by this technique. On careful examination the myelin sheath was detected. The reason why the sheath was not seen so readily by the gold technique on these nerves as in the nerves going to the *terminaisons en plaque* was that they do not take up the stain so heavily. Figure V is from a photomicrograph of a typical medullated fibre which proceeds to a *terminaison en plaque*, while Figure VI is that of one going to a *terminaison en grappes*. The significance of this observation will be discussed below, where the significance of this type of termination is considered. Other observations were made with regard to these grape-like endings, some of which were contrary to the findings of Kulchitsky. These were that *terminaisons en grappes* may be hypolemmal or apparently epilemmal, may be immediately connected with finely medullated nerves or apparently non-medullated nerves and may have primitive sole plates. They occurred on muscle fibres of widely varying diameter, which could be shown to receive no other innervation. With regard to the size of the muscle fibres, the typical *terminaisons en grappes* were observed on fibres ranging in diameter from 10 μ to 60 μ and the typical *terminaisons en plaque* on fibres of 90 μ to 150 μ in diameter.[1] Also the muscle fibres were often noticed to be grouped in bundles of various diameters. From the above observations it was concluded that many of the *terminaisons en grappes* could not be sympathetic in origin, but probably represented developmental forms of the ordinary motor terminations.

An attempt was made to record the various observations mentioned above by photomicrographs: these are reproduced in the accompanying figures. This was no doubt a somewhat ambitious procedure, for in photographing teased preparations it is obviously impossible to focus at once all the structures seen in any particular field. Tissues prepared by

[1] It must be pointed out that these measurements are only relative, for the fibres are pressed and are also somewhat swollen owing to the treatment to which they have been subjected.

the gold technique show great variations in density of stain and in colours, which range from pale pink to deep reds and purples. These facts account for the lack of resolution shown in some of the photographs, but in spite of this lack of clearness they form more reliable evidence than diagrammatic reproductions.

In some cases, however, the untouched photographs were quite unsuitable, because sufficient structural detail could not be reproduced, although the points illustrated could very readily be made out under the microscope. In a few cases, therefore, drawings are submitted and in other cases the photographs were slightly retouched. There was no hesitation in submitting these retouched photographs, as they have simply been included to help the argument and similar conditions have been fully described and figured by earlier investigators.

Figures I and II show typical sprays of plate-like and grape-like endings, respectively and Figures III and IV show the typical *terminaisons en plaque* and *terminaisons en grappe* under a higher magnification.

Figure VII shows the definite attachment of the *terminaisons en grappes* to the sarcolemma as do Figures XIV and XV. In these preparations tension on the fibre has pulled the sarcolemma up into a cone. In Figure VIII a *terminaison en grappes* is seen to arise as an ultra-terminal collateral out of a *terminaison en plaque* and, in Figure IX, a *terminaison en grappes* is seen on the end of a terminal collateral of a motor nerve, which ends in its typical plate. The fine muscle fibre in this latter figure is an intrafusal fibre of a muscle spindle, whose annular ending is well seen in the preparation in a field slightly to the left of this figure. Figure X is of another interesting specimen in which is seen a typical motor plate from whose fibre a medullated collateral arises and terminates in three sprigs of grape-like endings, lying in relation to two muscle fibres. No sole-plates were seen in relation to the grape-like endings in Figures X and XI.

With regard to the presence of sole-plates in relation to *terminaisons en grappes,* one is seen in the upper terminations in Figure II. This is shown under higher power in Figure IV. The small bundle of fibres in Figure II is made up of finely medullated nerves which are branches of the fibres in the coarser medullated bundle in the lower left-hand corner of the figure.

In Figures XII to XV various stages in the development of the motor endings are seen. The earliest form is not figured, but consists simply of a bead on the end of a fine non-medullated collateral of a non-medullated nerve, similar to the ultra-terminal collateral seen in Figure XVII. The earliest form figured (see Figure XIIM) has seven of these little beads lying in relation to a fine muscle fibre, which has a diameter of only 16 μ. In Figure XIII three stages can be recognized in the one field, from an early form in relation to a 16 μ muscle fibre (a), to a larger *terminaison en grappes* on a 70 μ muscle fibre (c). In figure XIV four stages are illustrated, namely (*a*) a grape-like ending on a 50 μ fibre, (*b*) an ending on a 60 μ fibre, (*c*) a large *terminaison en grappes* derived from a medullated nerve fibre and (*d*) a large *terminaison en plaque* on a very large 140 μ muscle fibre.

In Figure XV there are two of the late stages in development. Plate (a) is supplied by four fibres, one of which is medullated, the other three being non-medullated, but these latter arise from medullated nerves. Plate (b) is a large *terminaison en grappes* of a large medullated fibre, lying in relation to a very large muscle fibre. Tension on the nerve fibre has pulled up the sarcolemma of the muscle fibre. Figure XVI also shows an almost fully developed motor plate.

Another and very important observation is recorded in Figure VIII. This figure shows a *terminaison en grappes* on an ultraterminal collateral arising in a *terminaison en plaque.* These two figures (VIII and XIX) show the condition of ultra-terminal collaterals arising out of a plate on one muscle fibre and ending in another muscle fibre. As the existence of this condition has been denied by some, it is important to record it.

In Figure XVII another ultra-terminal collateral is seen ending on the same muscle fibre as does the plate from which it arises.

These series of figures seem to indicate the probability that at least some of the *terminaisons en grappes* are immature forms of somatic motor plates and, moreover, illustrate the various stages in the development.

It is necessary to point out, however, that although the grape-like endings are here regarded as immature motor endings, it is not implied that they will necessarily eventually develope during the life of the animal into plate-like endings. Whether they are endings which represent a reserve and can under certain conditions develope into plate-like endings or are endings in which development is definitely arrested, cannot be stated with any certainty. All that can be said, is that these grape-like endings can be arranged in a series which shows an increasing degree of resemblance to plate-like endings, and for that reason are here called immature motor endings. The condition of affairs, however, found in mammalian embryonic material and in young mammals and also in material from nerve regeneration experiments, seems to lend support to this conception, as will be seen later.

These conclusions also received confirmation from a different source and the observations about to be described serve further to confirm observations recorded by Perroncito[14][15] and which have not been generally appreciated. These were that the intrafusal fibre of the reptilian muscle spindle not only has the familiar annular afferent endings lying in relation to it, but also receives a supply from an efferent or motor nerve. This motor nerve fibre is a collateral of a motor nerve which is seen terminating on an ordinary extrafusal fibre in its

typical plate-like ending (see Figure IX). This latter connexion leaves no doubt as to its motor nature.

These collaterals of motor nerves to intrafusal fibres of muscle spindles show all stages of development of motor plates from single bead endings to quite large *terminaisons en grappes*, containing up to as many as a dozen beads.

The immature nature of these motor grape-like endings is further reflected in the fact that the staining reaction of their fibres to gold is not so marked as in the case of the fibres going to *terminaisons en plaque.*

These immature forms again are usually seen in groups showing various stages of development. When such a group of immature endings, such as is shown for example in Figure XIII, is examined, it is seen that the most immature forms are represented merely by a spray which arises from only one fine non-medullated fibril. The medium-sized *terminaisons en grappes* are, however, supplied by two or more non-medullated fibrils which on being traced back, are seen to arise eventually from two or more different medullated fibres. It is thus seen that an ending receives contributions from more than one medullated fibre. This observation is worthy of special emphasis, as it leads to the inevitable conclusion that medullation of the bundle of fibrils going to these endings must result in a plexus formation and it is important because it offers a further possibility with regard to the plurisegmental innervation or control of a muscle. A more detailed description of this observation, however, and a fuller discussion of the possibilities it opens up, are given below in the section dealing with plurisegmental innervation of muscle fibres.

Sensory "Terminaisons en Grappes" in Lizard Muscles.

From the observations recorded above, it appears very probable that many of the *terminaisons en grappes* represent immature forms of the motor plates, but there is evidence that afferent fibres may also have endings which can be described as *terminaisons en grappes.* These were observed in immature forms of muscle spindles. In the absence of degeneration experiments the nature of the endings seen in the very immature muscle spindles could not be definitely identified, but, however, in more advanced forms the presence of the typical annular endings is sufficient to enable one definitely to identify the afferent fibre. In these muscle spindles which show a more or less intermediate stage of maturity, the medullated afferent nerve fibre approaches the single intrafusal fibre of the muscle spindle somewhat near its equator and then divides dichotomously. The two primary branches thus formed pass towards opposite ends of and more or less parallel to the intrafusal fibre. These branches are at first medullated and have nodes of Ranvier at rather frequent intervals. From these nodes arise short non-medullated collaterals which end in relation to the intrafusal fibre. These endings often show various stages of development of annular endings. Thus, near the equator of the spindle the ring-like endings are fully developed, while further away from the equator they are of the nature of *terminaisons en grappes.* The two primary medullated branches which run parallel to the intrafusal fibre, also eventually lose their myelin sheath and end in *terminaisons en grappes.* It is thus definitely shown that at least some of the grape-like endings seen in reptilian muscle are afferent. Besides these *terminaisons en grappes* in muscle spindles, however, there were others lying among the ordinary muscle fibres which did not present the same picture as the immature motor forms described above. There was no suggestion of sole plates on the muscle fibres and the endings, although large, were apparently epilemmal and formed no attachment to the muscle fibres, for when the cover slip was pressed, the endings moved over the muscle fibres without causing the formation of a cone as described above. It seems that these should be regarded as endings of afferent nerves.

It is therefore concluded that *terminaisons en grappes* in lizard muscle are not to be regarded as a particular functional type of nerve ending.

Sympathetic Nerves in Lizard Muscles.

As it has been shown that *terminaisons en grappes* can be either endings of motor or of afferent nerves, the question arose as to whether any *terminaisons en grappes* were derived from sympathetic nerves. As sympathetic nerves supply blood vessels, these were examined to study the relation of the nerves there.

Figures XXXV and XXXVI show the sympathetic nerves lying on either side of one of the smaller blood vessels. Small branches from these nerves form a plexus from which little terminal branches arise and end in relation to the circularly disposed plain muscle fibres in the vessel wall. These ultimate endings are very small indeed and although they are bead-like, they are many times smaller than the beads of the *terminaisons en grappes* described above.

As the blood vessel divides into smaller and smaller branches, they are still accompanied by the sympathetic nerves which can be traced until the capillaries are reached. The capillaries sometimes have two fine nerve fibres accompanying them, one on either side, and sometimes there is only one. If these are traced, they eventually disappear out of microscopic vision. Sometimes the fibre leaves the capillary and wanders away across the muscle fibres, but almost invariably it can be traced on to another capillary, along which it can be followed till it disappears from view. In tracing these sympathetic fibres, none was observed to give off collaterals which ended in relation to the muscle fibres, so it was concluded that if the muscle fibres were innervated by the sympathetic, the sympathetic fibres apparently did not approach the muscle fibres from those nerves accompanying the blood vessels.

There was still the problem whether sympathetic nerves accompanied the somatic fibres and whether any of the *terminaisons en grappes* were sympathetic in origin. With regard to the latter, there were no *terminaisons en grappes* observed which could be distinguished from the immature motor or the sensory forms and none was observed to present relations similar to those figured by Boeke, namely, ending in relation to the sole plate of a motor termination.

Finally, to demonstrate the spinal cord origin of all the *terminaisons en grappes*, and to leave only sympathetic nerves in the lizard muscle to be examined, an attempt was made to throw all the nerve fibres of spinal cord origin into degeneration. The spinal canal of a lizard, therefore, was opened and the roots of the spinal nerves of five thoracic segments were cut near the cord, and also beyond the posterior root ganglion, and the pieces were removed. After four weeks the tissues were prepared, but showed no sign of degeneration. It was quite evident that a longer time must be left for degeneration. Operations were performed on other lizards, but it was difficult to keep them alive longer than five weeks. The attempts to verify by experiment the above conclusions with regard to the somatic origin of all of the *terminaisons en grappes* in the lizard have thus up to the present ended in failure.

Boeke,[16] however, performed a similar operation on a snake. In the snake, the skin is softer and more easily kept together after the operation, so that it is not so difficult to prevent infection. When Boeke examined the muscle taken from this snake three months after the operation, he found that the *terminaisons en grappes* showed signs of degeneration. These observations, combined with those made on lizard muscle in the present investigation, offer very strong evidence that in reptiles *terminaisons en grappes* are of somatic and not of sympathetic origin.

The only undoubted sympathetic fibres seen in lizard muscle are those seen in relation to blood vessels and in no case are branches from sympathetic nerves on blood vessels seen to pass on to end in relation to muscle fibres.

No evidence from histological methods, then, is found to support the contention that any of the *terminaisons en grappes* are other than endings of either somatic motor or of somatic afferent fibres.

One interesting observation, however, was made on the relation of the capillaries to the motor plates. Sometimes the capillaries were seen to form what may be called a *confluens capillorum*. This is shown in Figure I, especially in the plate to the left of the field, but also in two of the other plates. The significance of this is further discussed below in the general discussion on the sympathetic innervation of striated muscle.

"Terminaisons en Grappes" in Muscles of Python.

The preparations of python muscle examined came from only one python (*Python spilotes*) and our findings generally were substantially the same as those of Kulchitsky.[8]

Examination of the *terminaisons en plaque* in the python material investigated, however, revealed the fact that the sole plates were not well marked and also that the ramification of the axone in the sole plates did not present the broad fucoid fronds as in the lizard plates (see Figure III), but resembled more the stage in the development of the lizard's plate such as is shown in Figures XV and XVI. Here the individual fronds resemble more the bead-like endings of the *terminaisons en grappes* or the leaves of maiden hair fern. Terminal collaterals and ultra-terminal collaterals like those seen in lizard muscle were observed. The age of the python was not known.

With regard to the sympathetic nerves the evidence pointed to the same conclusions as those arrived at in the case of lizard muscle, that is that sympathetic nerves merely supply the blood vessels.

Before the consideration of reptilian muscle is left, it should be recorded that no evidence was found to confirm the observation of Dart[17] that small, grape-like terminations embrace the small blood vessels. As Dart was examining teased material he probably observed *terminaisons en grappes* that had become pressed against a blood vessel during the course of the preparation of the specimens. If such endings existed in relation to blood vessels, we must have seen them, as we have carefully examined hundreds of good preparations.

"Terminaisons en Grappes" in Frog's Muscle.

The tissues of several frogs were examined and the motor plates were seen in all stages of maturity from *terminaisons en grappes* (Figure XX), through the simple filiform types of motor plates (Figure XXI), to the coarse fronded, elongated plates as seen in Figure XXII.

The ending shown in Figure XX is at the end of a fine fibre which can be traced back until it is seen to be a branch of a large fibre which ends in several typical filiform motor plates. Careful examination of the preparation shows that one large motor fibre branches frequently and ends in relation to several muscle fibres of different diameters; the endings of the various branches show different stages of development. Moreover, ultra-terminal collaterals occur frequently and sometimes one muscle fibre is seen to receive endings of more than one terminal branch. Figure XXIII shows such a condition, in which an ultra-terminal collateral of one ending terminates on another muscle fibre already supplied by an ending. Such observations show a more general, instead of a particular relation of nerve fibres to muscle fibres. This is of particular phylogenetic interest and suggests the gradual development of a more specific innervation of muscle fibres from a more general innervation. Similar observations were made in salamander muscle tissue. It is even possible that the variety of forms of motor plates in amphibian and reptilian muscle may rather represent phylogenetic than

ontogenetic immature forms. However this might be, the preparations of frog and salamander tissue showed that where the muscle fibres varied most in diameter, there the immature forms were of most frequent occurrence. In some of the preparations of salamander tissue there seemed to be a great deal of overlapping of nerve endings on muscle fibres and this occurs especially where the fibres varied greatly in diameter. Here the medullated nerve fibres gave off numerous fine non-medullated branches, besides the usual medullated ones and formed almost a riot of nerve endings among and on the muscle fibres and frequently showed ultra-terminal collaterals.

Returning to frog's muscle, besides the motor *terminaisons en grappes,* many were afferent, since they were seen to come off branches of the sensory fibres going to the muscle spindles. The muscle spindles in the frog have several intrafusal fibres, thus differing from those in the lizard and snake which have only one or two, and the large sensory nerve which supplies a spindle, ends in an elaborate terminal arborization, the numerous and elongated branches of which lie in close relation to the group of fine intrafusal fibres. These fine terminal branches end in little bead or grape-like structures so that the whole structure looks like a very elaborate *terminaison en grappes.*

Sympathetic nerves on blood vessels were readily stained both with the gold and methylene blue methods, but although a very exhaustive search was made, no relation with muscle fibres could be discovered.

Observations on a Muscle Preparation of the New Zealand Sphenodon or Tuatara Lizard.

Through the courtesy of one of our technicians I was able to examine one slide of a teased preparation of a piece of muscle tissue from the tuatara. Figure XXIV shows a typical mature motor plate. This photograph was taken under the same conditions as Figure I, so one may see the large size of the plates in comparison with those of the lizard. These endings look very much like the motor endings seen in snakes and in birds, all of which have motor plates that look more beaded than the broad fronds of the mature frog, lizard and mammalian plates.

Two other endings in the tuatara muscle preparation are shown in Figures XXV and XXVI. In Figure XXV the plate is supplied by two fibres, both of which are medullated. Figure XXVI is a very small grape-like ending in relation to a comparatively small muscle fibre. There is no doubt that in the tuatara the same conditions obtain as have been described in the frog and blue tongue lizard.

"Terminaisons en Grappes" in Mammals.

On searching through the muscle preparations of various mammals no *terminaisons en grappes* were at first found. The only type of ending seen was the ordinary *terminaison en plaque.* In small muscles, such as the lumbrical of the foot in which it was possible to mount the whole muscle at once, the only type of ending seen to be in relation to the muscle fibres were *terminaisons en plaque.*

This fact is important and it is especially necessary to emphasize it, for Hunter and Latham[10] have published what they thought was evidence of the existence of efferent *terminaisons en grappes* in mammalian muscle. The evidence of Hunter and Latham seemed at first difficult to understand; however, on carefully going through their work it was found that they had found this type of ending only in the extrinsic eye muscles of the goat. When their work was repeated and large pieces of muscle were mounted, it was discovered that the *terminaisons en grappes* found in these muscles arise from an extensive plexus of medullated nerves. So numerous were the branches of these nerves that almost every muscle fibre had one or two or more terminal branches lying in relation to it. Sometimes a fine nerve would run almost the complete length of the muscle fibre, giving off little sprays of grape-like endings at short intervals. Figure XXX shows a typical spray of motor plates in an extrinsic eye muscle of a rabbit. But besides these motor nerves and their endings, there are seen numerous fine non-medullated nerves lying in relation to the muscle fibres. Only a few could be focused and photographed at once. This preparation, however, shows a remarkable plexus of medullated nerves from which these fine nerves take origin. The nerves which form the plexus, are not so coarse as the motor nerves shown in Figure XXX. Figure XXXI shows another field in which the fine nerves are more numerous, and Figure XXXII is a drawing of a smaller, more finely teased preparation. A similar plexus of fine nerves with its fine terminal filaments was seen in the other eye muscles examined. On reviewing the literature, it was found that these endings had been observed and fully described by earlier investigators.

Apparently they were first described in 1892 by Retzius[18] who called them "atypical motor endings." Huber,[19] however, in 1899 by very careful histological examination of these endings not only in teased preparations, but in preparations cut in longitudinal and transverse sections, came to the conclusion that these so-called "atypical endings" of Retzius were sensory (afferent). Dogiel[20] in 1906 extended and confirmed Huber's observations and also concluded for the same reasons that these endings are afferent.

As further evidence of the sensory nature of these endings in eye muscles may be mentioned the fact that, on teasing out fasciculi of muscle fibres from these eye muscles, every muscle fibre appeared to be supplied in addition by an ordinary motor ending.

All the evidence seems to point to the conclusion that these endings are afferent.

It is especially necessary to appreciate fully the significance of these endings, because Boeke's chief evidence of the sympathetic innervation of striated muscle is based on degeneration experiments on one

of these extrinsic eye muscles. (See section on sympathetic nerves in striated muscle of mammals.)

The same remarks apply to tongue muscles. Here the sensory terminations are also very plentiful. Just as is the case in eye muscles, a very elaborate plexus of medullated sensory nerves gives rise to most extensive terminal arborizations, the branches of which lie not only in relation to the muscle fibres, but in the corium under the stratified squamous epithelium, especially in the papillæ, also actually among the epithelial cells themselves.

Similar elaborate terminal arborizations of sensory nerves were also noticed under the serous surfaces, for example, under the pleura, and some of the fine terminal branches were seen to go down among the muscle fibres of the intercostal muscles. The first of such sensory terminations was noticed under the peritoneum on the anterior abdominal wall of the frog, in a preparation prepared by the methylene blue technique and this led to the investigation of similar endings in the mammal. As the terminal branches of these sensory arborizations are non-medullated and give rise to grape-like or bead-shaped terminations, it is quite possible that they represent a source of fallacy when sympathetic nerves are sought in intercostal muscles. There is a possibility also that these sensory nerves are not arranged segmentally or, if they are, they may overlap several spinal segments so that they may remain intact in degeneration experiments carried out on intercostal nerves, when only three or four intercostal nerves are cut.

In a lumbrical muscle of a rabbit's foot a sensory ending was noticed which was of the nature of a very elaborate *terminaison en grappes*. It was a structure somewhat similar to a Golgi ending in tendon, except that it ended in the connective tissue between the muscle fibres. It is interesting to mention this and it might also lead to false deductions in searching section preparations of this muscle for evidence of sympathetic innervation.

Discussion.

The foregoing observations on *terminaisons en grappes* seemed to suggest that the bead-like ends of the terminal branches of an axone represent the growing ends of nerves. In the case of the lower vertebrates they represent immature forms of the motor and the sensory endings, growing out to establish relations with peripheral structures. The process may be roughly compared to the protrusion of long fine pseudopodia with bulbous ends such as are sometimes put out by cells which exhibit amœboid movement. In the one case there is the budding of motor nerves to establish relations with developing muscles fibres, and in the other case the sensory nerves are growing out not only to keep pace with the growing tissue, but probably in response to alterations in the demand for sensory nerves. For it seems to me that a dynamic relation of sensory nerves to peripheral structures is more reasonable than a static one. With continual readjustment of the animal organism to environment there is a continual budding and growing of sensory nerve endings to establish more satisfactory relations with peripheral structures. When nerve endings become encapsulated, this process is checked, but while the sensory nerves form free endings in the tissues, they can sprout and grow, not only to establish new relations to meet the demands of the growth of the organism, but possibly also to replace worn-out or damaged twigs. But even when endings are encapsulated, for example, in Pacinian corpuscles, the end of the axone is still capable of growing out the distal end of the corpuscle and eventually giving rise to other Pacinian corpuscles, as the organism grows, to meet the demands for more satisfactory reception of stimuli. To put it in another way, there seems to be a mechanism whereby the sensory nerves grow in response to stimulation and in the case of motor nerves growing out into developing muscles there seems to be a "call" from developing muscle fibres to motor axones, resulting in the branching of the axones affected.

With regard to this question of the growth of nervous tissue in response to stimulation, Agduhr[21] in his researches on postnatal development of the nervous system has observed active division of ganglion cells in the spinal root ganglion of very young actively growing animals and has also recorded a definite increase in the number of nerve fibres in spinal nerves when the animals were subjected to a gradually increasing amount of exercise extending over some months. Further, examination of the nerve trunks in longitudinal section also revealed the bulbous or beaded ends of the new fibres growing peripherally.

The same kind of mechanism is also seen in the central nervous system itself, as witnessed by the existence of bead-like terminations on the ends of the axones at a synapse. The work of Ariëns Kappers and Davidson Black has made us familiar with the principle of neurobiotaxis which is an attempt to account for the position of the motor nuclei in the brain stem *et cetera,* but prior to the movement of cytons in the direction from which they receive their principal afferent impulses, there must first be a growing out of the afferent axones to establish relations. Both in phylogeny and in ontogeny there is a general tendency or "striving" on the part of organisms to adjust themselves to their environment and this is structurally registered by a continual and progressive adjustment between the afferent and efferent side of the nervous system. The organism which retains the potentiality for some such continual readjustment, instead of becoming set with regard to any particular neuronic pattern, has a greater chance of survival and of progress from the point of view of evolution. The phenomena of effort and of attempt at adjustment with environment, whether unconscious or conscious, are mental phenomena and are an index of mind and such mental phenomena are structurally or

neurologically registered by a growing out of axones until they establish those relations which provide a mechanism of suitable response. As these relations are being established, the principle of neurobiotaxis also applies and accounts for the ultimate relation of cytons to form the aggregates called nuclei in neurological architecture.

Remarks on the Structure of Somatic Motor Endings in Mammals et cetera.

Modes of Termination of the Motor Nerve Fibres.

Before proceeding to the discussion of the sympathetic innervation of striated muscle, it is first necessary to mention a few points in connexion with the structure of somatic motor endings, for just as *terminaisons en grappes* have led to confusion in investigations on this problem, so has some confusion arisen from the occurrence of infrequent variations in the mode of termination of the somatic motor nerves.

Reference has already been made to the occurrence of terminal and ultra-terminal collaterals which have been observed in the striated muscle tissue of cold blooded animals. The term terminal collateral is used to describe the condition in which a medullated somatic motor fibre gives off at a node of Ranvier a fine non-medullated branch which accompanies the parent fibre and terminates with it in the same sole plate of a muscle fibre. In normal tissue where this branch is long and where the tissue is cut into sections, it may not be possible to trace this fine branch to its ultimate source. Writers have suggested that this may represent a source of fallacy when a fine fibre is figured ending in a sole plate alongside the typical ending of a somatic motor nerve and which is claimed as a sympathetic accessory fibre.

An ultra-terminal collateral is a fine non-medullated nerve fibre which arises as a branch of the axonal ramification in a typical somatic motor plate and ends either on the same motor fibre at some distance from the plate of origin or ends on another muscle fibre. In sectioned material in which such endings occur, the source of the fibre may be lost and it has been suggested that this also is a source of fallacy when sympathetic endings in normal tissue are looked for.

In my observations I kept a constant look-out for the occurrence of these collaterals, but although they were more frequently seen in frog and salamander tissue, they were only occasionally seen in lizard tissue, while in mammals, although a very great number of plates was seen, I failed to find any ultra-terminal collaterals and the terminal collaterals seen were very short.

In the interosseous muscle of a cat a classification of some 500 endings was made and with the following result. In over 90% of cases the motor fibre retained its myelin sheath up to within about 10-15 μ of the plate. From here the axone passes into the sole plate and ends in its typical ramification. The neurilemma sheath which is retained, becomes continuous with the sarcolemma of the muscle fibre. Figure XXXVIII is a *camera lucida* drawing of such a typical normal ending.

In other cases—less than 10%—the following variations were found (see Figure XXXIX). The motor nerve divides at a node of Ranvier into two short terminal branches both of which may be medullated (*a*) or one may be medullated and the other non-medullated (*b*) or both may be non-medullated (*c*). Also sometimes there were more than two terminal non-medullated terminal branches (*d*). In no cases were the terminal branches of the axone very long; the longest was 35 μ. These were in general the only type of variations seen in mammalian muscle tissue.

Another interesting observation was made on the structure of the neurilemma sheath, especially that part which covers the axone after it has lost its myelin sheath, and also that part which covers the sole plate. In these situations it is seen to have little structures which look very much like the varicosities of fine non-medullated nerve fibres (see *v*, Figure XXXVIII). Also sometimes the neurilemma sheath over the medullated nerve is seen to be wrinkled and the folds receive a little deeper impregnation in the staining process. It may be that the fibres of Henle's sheath sometimes account for the appearance. These deposits, then, together with the little structures first mentioned, may give rise to the false impression that the large medullated nerve fibre is accompanied by a finer non-medullated varicose fibre or fibrils. These could not be successfully photographed, but the drawing in Figure XL will convey the idea.

Such artefacts were never observed in preparations stained with methylene blue.

The Structure of the Motor End Organ.

By the gold and methylene blue techniques the axone was seen to end in the sole plate by branching into a number of coarse fronds. The finer reticular nature of these fronds is not disclosed by these methods, as it is by the various modifications of the Bielschowsky silver technique. Also by these techniques the edges of the fronds appear clear cut and even in outline and their under surfaces are more or less flat. Also the sarcoplasm of the sole plate is clear and unstained by methylene blue, while with gold it has a fine granular appearance throughout except close to the fronds. The fronds in the gold technique then are separated from the granular sarcoplasm by a clear area (see Figures I, III, XXXVII) and the nuclei of the sole plate remain unstained. By the silver technique in some preparations the fronds of the axonal ramification appear as a neurofibrillar reticulum. Sometimes, however, the edges of the fronds appear dentate and their under surfaces are thrown into folds. The sarcoplasm in these cases appears as a "foam" or "vacuolated" structure which is identified by reason of the fact that the silver is finely deposited between the "vacuoles." This inter-vacuolar deposit gives rise to the appearance of a palely stained reticulum which appears to be continuous with the reticulum

of the fronds. This appearance was first described by Boeke[22] who called it a periterminal network. Boeke, however, obtained his best results after a very prolonged fixation in formalin, namely, four months and much longer, and moreover counterstains his preparations with hæmatoxylin. This counterstaining makes the periterminal network more distinct, but after a time it tends to fade out. While with Boeke, I was shown such a preparation, but the periterminal network had almost faded out.

All Bielschowsky preparations, however, do not present the sarcoplasm of the sole plate as a foam structure and in these cases there is no distortion of the fronds and no periterminal network continuous with the reticulum of the axonal fronds. I have seen the beautiful silver preparations of Murray,[23] Agduhr and Bielschowsky and in none of them is this periterminal network to be seen, except in Murray's and even in his it was only very occasionally seen. Murray's preparations, however, were also counterstained with carmalum.

With regard to the actual structure of the periterminal network it looks distinctly granular in appearance and is not at all comparable to a neurofibrillar reticulum. I cannot help thinking that this structure is an artefact due to the method of fixation. Moreover, we must draw a line somewhere, for if all argentophile substance is to be regarded as nerve-conducting, then all tissues would come in this category.

In well fixed, well stained silver preparations in which the various tissues are well differentiated, the nerve endings appear as sharply defined, definitely circumscribed, undistorted reticula.

Note on Krause's Membrane.

While the question of the structure of motor end organs is being discussed, it is not altogether out of place to digress from the main subject of this paper and to insert a few remarks concerning the infrafibril mechanism for the propagation of the effector impulses. With regard to the view, therefore, put forward by Tiegs,[26] no evidence could be found for the existence of connecting fibrils between the fronds in the ramification of the axone and Krause's membrane. Tiegs first based his evidence on an observation made in a section of muscle tissue prepared by the gold technique, which showed the nerve ending in profile, and while it must be admitted that conclusions based on one accurate positive observation may sometimes outweigh that based on any number of negative ones, we have little doubt that in this case it has not been well founded. In tissues prepared by the gold technique the sole plates in relation to the nerve endings in muscle fibres appear to be composed of a granular protoplasm with nuclei, the nuclei, however, remaining unstained and appearing as clear areas (see Figures I and III). The protoplasm immediately in relation to the ramifications of the axone also appears clear and unstained. In profile the distribution of these clear areas in a deeply stained granular protoplasm often makes it appear as if there are connecting strands through the sole plate projecting down from the muscle face of the nerve ending, but from observations of a great number of such preparations no evidence could be found of a neurofibrillar structure in the granular protoplasm. Tiegs later believed he had confirmation of this observation in a piece of frog's muscle prepared by the methylene blue technique. The ending he figures, is a typical grape-like immature type of motor termination in which no distinct sole plate had appeared, and the little grape-like bodies lie under the sarcolemma and are arranged according to his figure in apposition to the membranes of Krause. This is quite a fortuitous arrangement and not to be regarded as at all usual. Many hundreds of nerve endings in muscle tissue, taken from all parts of a frog and stained by the methylene blue and gold techniques, have been examined and not one example was found which corresponded to that described by Tiegs.

The histological evidence based on a wide and extensive range of observations in all types of animals, all points to the conclusion that there is no neurofibrillar connexion between nerve endings and Krause's membranes. The physiological and pharmacological evidence also points to the existence of an intermediate substance between nerve endings and contractile tissue.

Tiegs[24][25][26] has also put forward the view that Krause's membrane is to be regarded, not as a series of parallel structures lying at right angles to the long axis of the muscle fibre, but as a double helicoid which acts as a path for conduction of the nervous impulse through the muscle fibre towards both ends, starting from the nerve ending which is usually situated towards its equator. This view and that discussed under the heading "Modes of Termination of the Motor Nerve Fibres" are both parts of Tieg's general conception of the mechanism through which a nerve impulse produces contraction of a muscle. He based his idea of Krause's membrane on the fact that in focusing from one side of a fibre down through to the other side the cross striations sometimes show a criss-cross appearance which he states could be produced only if the arrangement is regarded as a double helicoid. This is rather slender evidence on which to base such an hypothesis. We have noticed this effect that Tiegs describes, in fresh and in gold stained press preparations, but observations on many of our preparations show that bundles of sarcostyles in a muscle fibre show different degrees of contraction tending to a fragmentation of the cross striations. Many fibres also have frayed ends with the sarcostyles fanned out like a tassel, and many again manifest a tendency to split transversely between the sarcomeres at Krause's membrane. In paraffin sections where the fibres are cut accurately in longitudinal section, this appearance is not detected. There appears to be no reason to abandon yet the text book description of intramuscular structure as set forth, for example, in Schafer's "Histology."

According to a figure after Rollet, reproduced by Tiegs,[27] it would appear that when a muscle fibre contracts, the wave of contraction passes out fanwise from the region of the nerve ending and eventually passes down the muscle fibre at right angles to the long axis of the figure. This observation is more in keeping with the view that the influence radiates from the nerve ending through a fluid or semifluid medium, rather than along definite neurofibrillar conducting paths, as described by Tiegs.

Evidence has already been put forward to show that a nervous impulse can be propagated through a fluid or semifluid medium, for it has been shown by Bethe that when the neurofibrils of an axone are cut, there is no hindrance to the conduction of the impulse. Possibly, then, fine neurofibrillar strands with their relatively large surface compared with their bulk, may act merely as a directional mechanism. Once a nervous impulse reaches, for example, the nerve ending in a muscle fibre, it radiates out through the muscle fibre, causing contraction in the sarcostyles, as it passes across and along the muscle fibre. Krause's membranes may merely represent a supporting mechanism which among other things tends to preserve a definite orientation of the sarcostyles to one another and of the component units of the sarcostyles, namely, the sarcomeres.

Sympathetic Nerves in Striated Muscle.

It has already been noted that in the lower vertebrates, namely, amphibians and reptiles, no nerve endings were found in hypolemmal relation to the striated muscle fibres, except the ordinary *terminaisons en plaque* of coarsely medullated cerebro-spinal nerves and the *terminaisons en grappes* which, as is claimed above, represent immature forms of somatic motor endings. Further, in the various representatives of the mammalian orders examined from monotremes to man no fibres were found to end hypolemmally in relation to striated muscle fibres, except those that ended in the ordinary typical motor end plate. In other words, in mammals every striated muscle fibre was found to receive only the one type of motor ending.

The results of the present investigation, then, point to the conclusion that striated muscle fibres are not innervated by sympathetic nerves and that in striated muscle tissue the sympathetic nerves are concerned merely with the regulation of the circulation.

When the evidence for the sympathetic innervation of muscle fibres presented by some previous investigators is examined, however, it appears at first glance to be very convincing, but a more careful analysis of it brings to light certain difficulties. First may be mentioned the infrequency of the occurrence of Boeke's accessory endings. If they served any important function, such as that in relation to muscle tone, they would surely be found in greater numbers and without much difficulty. Boeke himself has found only a very few examples and, further, it is significant that the only investigators who have seemed to produce convincing evidence in support of his hypothesis, are Agduhr, Garven and Kuntz. On the other hand, there are other competent investigators, such as Bielschowsky, those of the Cajal school, Woollard and Hinsey, who have been unable to confirm Boeke's work. Finally, in the present investigation their detection has defied all efforts, although a great quantity of material has been carefully examined.

Again, another difficulty arises in regard to the question of the general morphology of the accessory endings, for one of the first general impressions obtained from a survey of the evidence, is that they appear to occur in a variety of forms and to exhibit no generally characteristic type of structure. First with regard to their size, it appears that they may occur either as a single end net, end loop or bead-shaped structure (Boeke,[5] Figure XV) or may be a much larger structure, composed of as many as nine of these end nets *et cetera* and occupying an area on the muscle fibre as large as and even larger than an ordinary somatic motor plate (Boeke,[5] Figures III, VI and XII, and Agduhr,[28] Figures IV, VI and VII). Also they may be located in sole plates of somatic motor nerve endings or at places some distance from these structures and in the latter case they are sometimes represented as ending in sole plates of their own or sometimes they have none. These sympathetic sole plates, when they occur, are figured as having anything from one to seven nuclei.

Another interesting fact and one that is difficult to understand, is that with regard to the "accessory" fibre. This is represented, even in preparations from the same muscle, as sometimes having varicosities (Boeke,[5] Figure I) and sometimes as being smooth in contour, that is, having no varicosities (Boeke,[5] Figure XV). Also the fibres figured by Agduhr in the interosseous muscles of a cat, are represented in some cases as being fine and varicose (Agduhr,[28] Figures I, III and VIII) and in other cases as being composed of quite a number of neurofibrils (Figures IV and VII).

Another point worth mentioning also concerns the histological relations of the accessory fibre in the muscle. The fibre has been variously described as arising from the plexus of nerves on blood vessels or as approaching the muscle fibre in company with somatic motor nerves or, finally, as pursuing an altogether independent course.

Although lack of uniformity *per se* cannot be regarded as evidence against the common identity and sympathetic nature of these accessory fibres and endings, yet it seems strange that structures, presumably performing similar functions, should vary so much in structure and even in one and the same muscle and it is not unreasonable to claim that in the final weighing of the pros and cons of this important question all these points must be taken into consideration.

With these general remarks we may proceed to examine the evidence in more detail.

Boeke's evidence of the sympathetic innervation of striated muscle is based chiefly on (i) the apparent occasional occurrence of accessory endings in or near sole plates of somatic motor endings and Garven[12] has reported similar observations and (ii) the apparent occurrence of hypolemmal endings in relation to striated muscle fibres after an attempt had been made to throw all somatic nerves into complete degeneration.

Evidence of Accessory Endings in Sole Plates.

With regard to the accessory endings in sole plates, it was mentioned above that in lizard muscle the blood vessels often formed a *confluens capillorum* (see Figure I) in the region of the sole plate of a motor ending. This offered a possible explanation of the apparent existence of sympathetic nerves in sole plates as described by Boeke. To ascertain whether this was more than a mere accidental occurrence, a rabbit's leg was injected with a mass used by Lee-Brown[30] in his investigation on the circulatory system and pieces of tissue from the various muscles were prepared according to the gold technique. The nerves and their endings stained very well and the relations of the blood vessels and capillaries were very well shown. In the preparations examined an unmistakable relation existed between the capillaries and the sole plates. A particularly good specimen was obtained from an interosseous muscle. In this the nerve trunk lay across the fibres approximately at right angles to their long axes and gave off branches on either side to the sole plates of the muscle fibres. This trunk was accompanied by the blood vessels which gave rise to the capillaries that ran off parallel to and alongside of the muscle fibres. These capillaries formed anastomoses with one another across the muscle fibres at frequent intervals, but the anastomosing branches were in special evidence in the two lines of the sole plates on either side of the main nerve trunk and many of the sole plates were the site of what we have called a *confluens capillorum.*

This relation of capillaries to sole plates was a very frequent occurrence in the rabbit's muscle tissue examined and if the sympathetic nerves which accompany the capillaries are traced, they are found to form very close relations with the sole plates and muscle fibres exactly as they are figured by Garven, the only investigator who claims to have demonstrated the sympathetic innervation of striated muscle by the gold technique.

In my opinion the sympathetic nerves figured by Garven[12] as ending in relation to the sole plates of muscle fibres, are no more than the nerves on the capillaries. There is one observation, however, recorded by Garven which calls for special criticism, and that is the one shown in Figure IX of his article. The following quotation from Garven's article is his description of the figure:

> One special case seems of still greater importance, that shown in Figure 9, in which an accessory fibre is seen ending in profile on a muscle fibre, after a short course from a leash of medullated and accessory fibres. The accessory fibre divides up into branches, most of which end in darkly staining end-knobs forming a small plate on the muscle fibre, while one of these branches pursues a downward course and becomes ultimately associated and connected with a capillary. This demonstrates conclusively that the accessory fibres which supply the capillaries, and those which have small end plates, are of exactly the same origin.

From an examination of muscle preparations similar to that described in this quotation we are inclined to think that the ending which he calls accessory, in this case is a somatic motor plate with an ultraterminal collateral which ends on the same muscle fibre as the plate from which it takes origin. The "downward coursing branch" appears intimately associated with the capillary, because the two are pressed together. Similar relations of small endings to capillaries may easily occur in teased preparations, but they are most probably artefacts. It is significant also that none of the other endings that Garven figures as accessory looks anything like this one. It is almost certain that it is not sympathetic at all. Apart from this figure, then, all Garven's figures show "accessory" (that is, sympathetic) fibres which can be considered as having relations to capillaries as described above.

The next step in the investigation was to see what relation the capillaries bore to the muscle fibres. Pieces of the injected muscle were put through the paraffin process in the ordinary way and examination of the sections revealed that the capillaries formed most intimate relations with the muscle fibres and it was difficult to see any structures whatever in between the injected mass and the substance of the muscle fibre. It was quite evident that only two layers of the thinnest possible protoplasmic membrane separated blood from muscle tissue and they were the attenuated epithelial cells of the capillaries and the sarcolemma.

It appears that in sectioned material it is quite possible to interpret nerves on capillaries as nerves passing to the muscle fibres and as the capillaries form such intimate relations with sole plates, it is quite possible that sometimes the sympathetic endings which are really on blood vessels, appear to lie in relation to the sole plates. If this is so, they may be explained by regarding them as growing ends of sympathetic nerves. Just as the relation of somatic nerves to peripheral tissues is a dynamic rather than a static one, so is the relation of capillaries and their sympathetic nerves to the tissues which they supply. New capillaries are being continually opened up and possibly old ones are continually disappearing, so the relations of the sympathetic nerves must be continually varying. As new capillaries open up, so sympathetic nerves grow out along them and it is quite possible that endings of nerves which are passing out along the growing capillaries, may occasionally be seen to lie apparently in close relation to cellular structures such as sole plates and in relation to nuclei of sarcolemma cells. It may not signify any more than that the sympathetic nerves grow towards points

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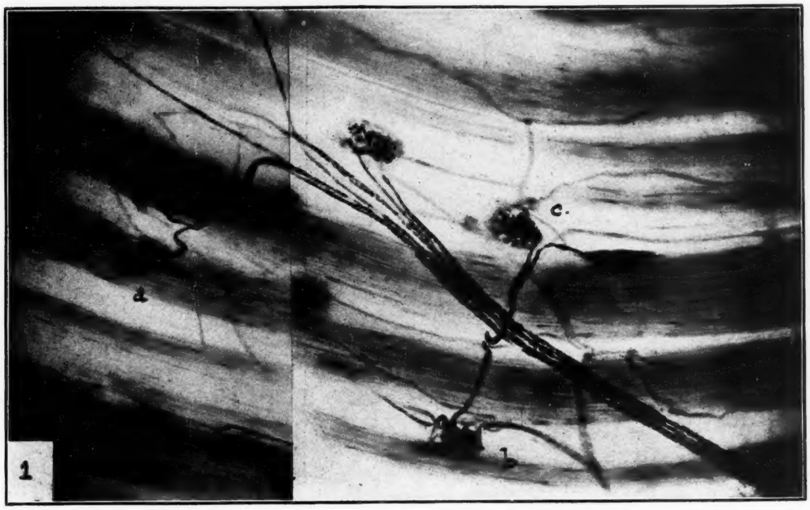

FIGURE I.

FIGURE V.

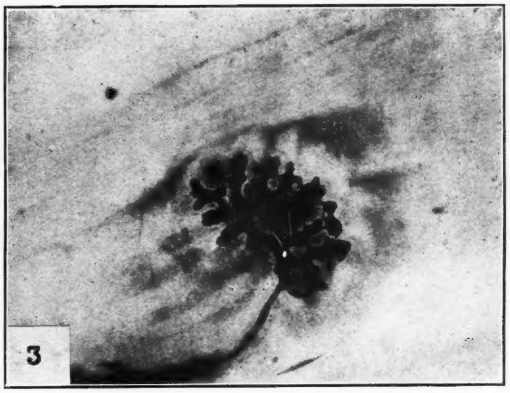

FIGURE III.

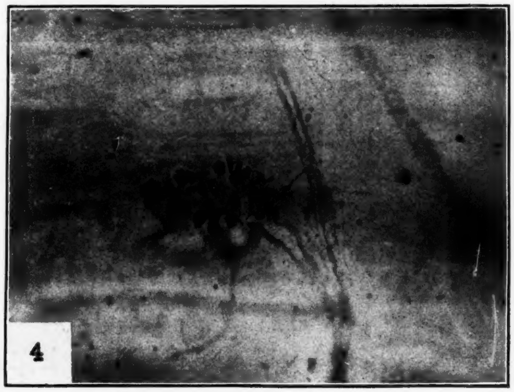

FIGURE IV.

FIGURE VI.

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FIGURE II.

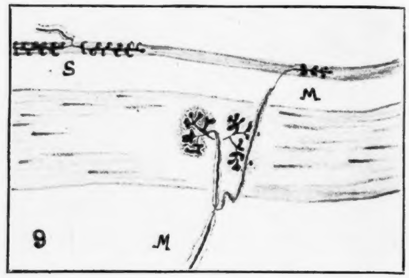

FIGURE IX.

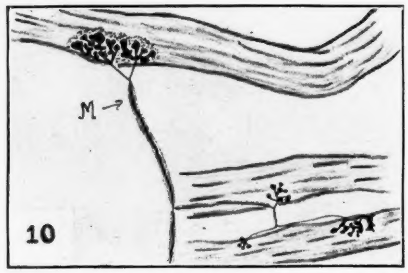

FIGURE X.

FIGURE VII.

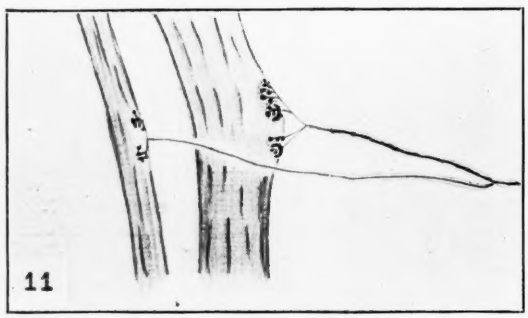

FIGURE XI.

FIGURE VIII.

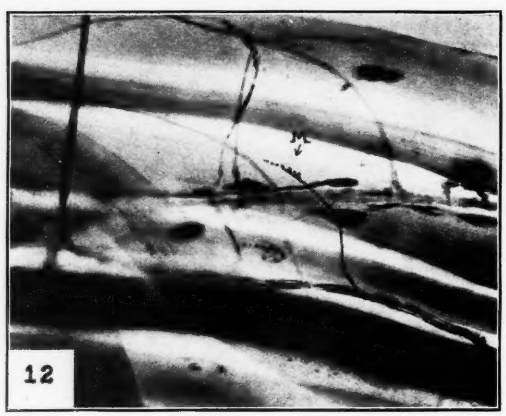

FIGURE XII.

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FIGURE XIII.

FIGURE XVI.

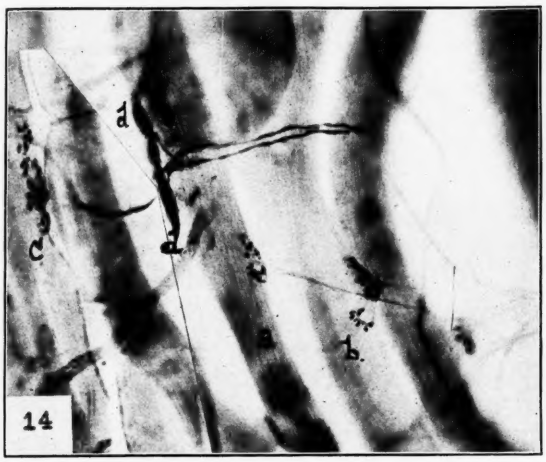

FIGURE XIV.

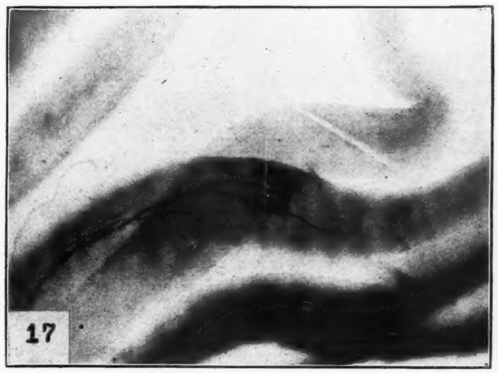

FIGURE XVII.

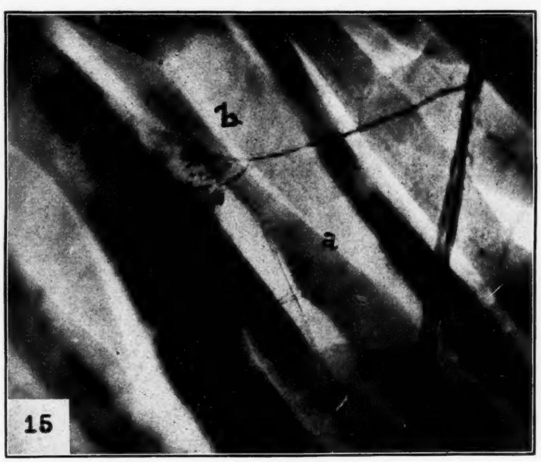

FIGURE XV.

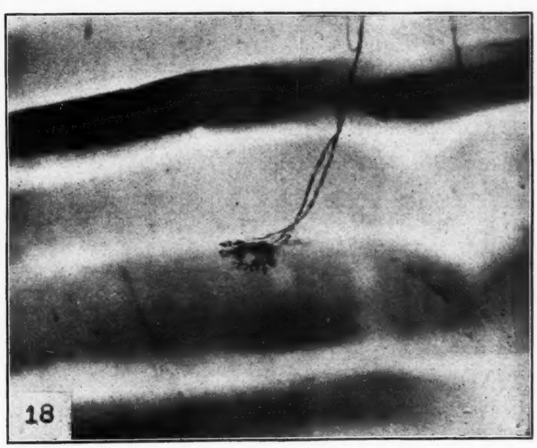

FIGURE XVIII.

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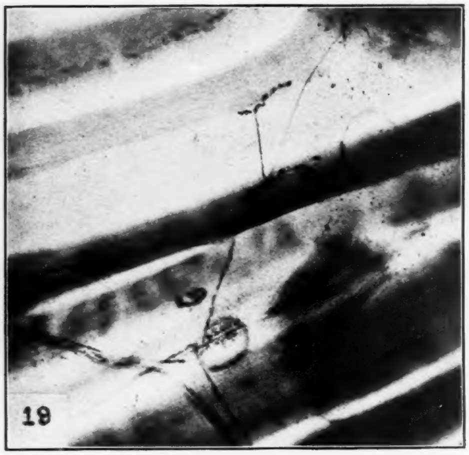

Figure XIX.

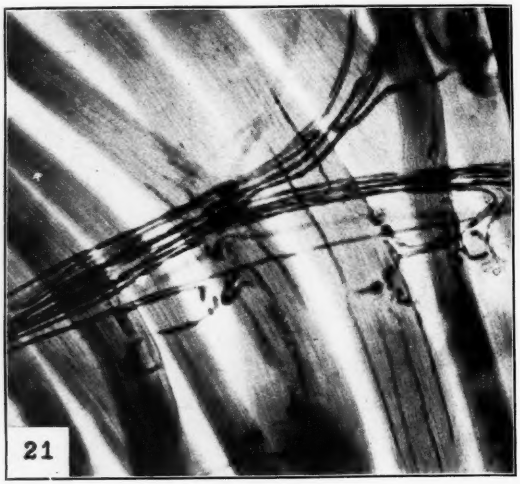

Figure XXI.

Figure XXII.

Figure XX.

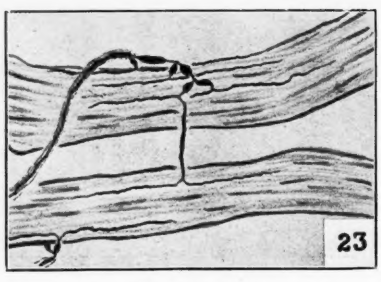

Figure XXIII.

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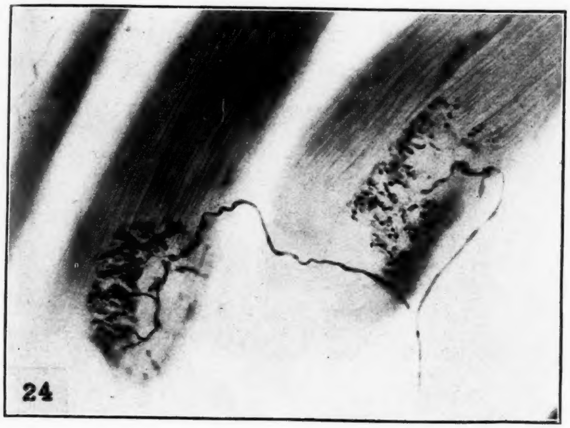

FIGURE XXIV.

FIGURE XXV.

FIGURE XXVI.

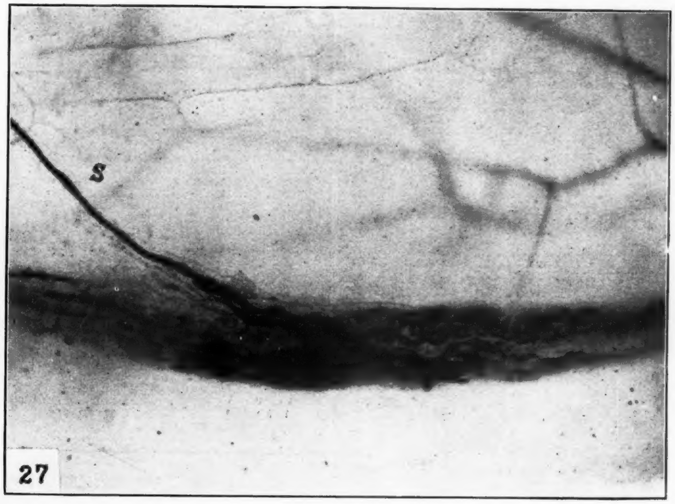

FIGURE XXVII.

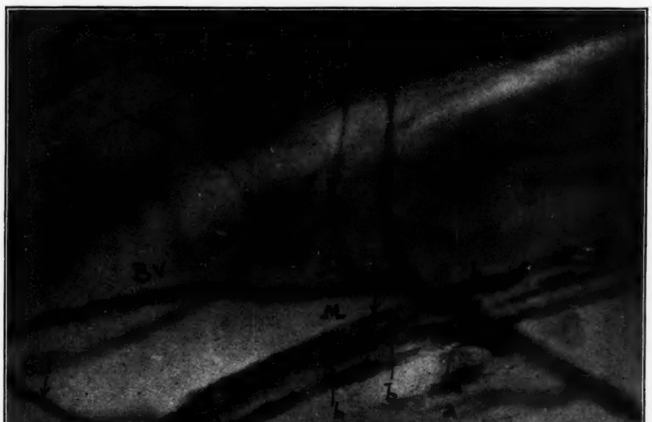

FIGURE XXVIII.

FIGURE XXIX.

ILLUSTRATIONS TO THE ARTICLE BY DR. HERBERT J. WILKINSON.

FIGURE XXX.

FIGURE XXXI.

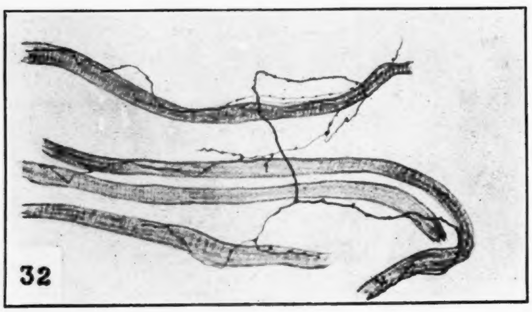

FIGURE XXXII.

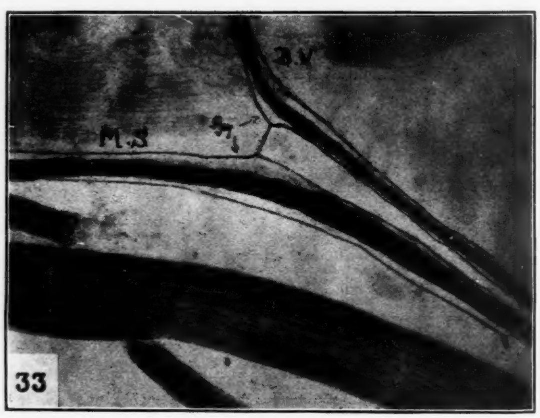

FIGURE XXXIII.

FIGURE XXXIV.

ILLUSTRATIONS TO THE ARTICLE BY DR. HERBERT J. WILKINSON.

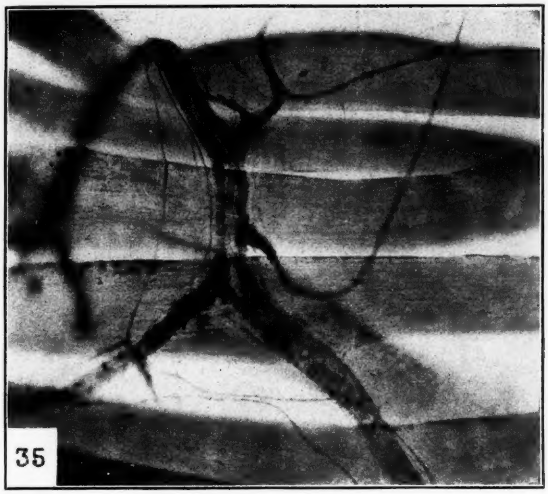

FIGURE XXXV.

FIGURE XXXVI.

FIGURE XXXVII.

ILLUSTRATIONS TO THE ARTICLE BY DR. HERBERT J. WILKINSON.

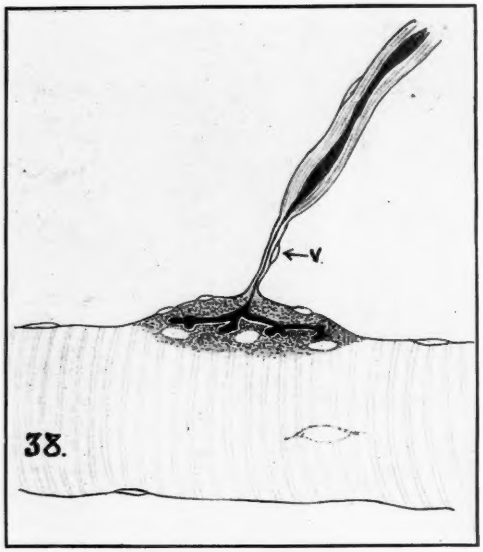

FIGURE XXXVIII.

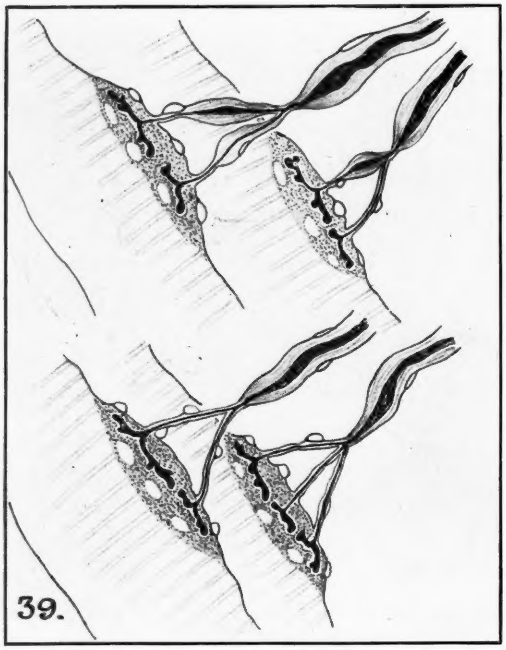

FIGURE XXXIX.

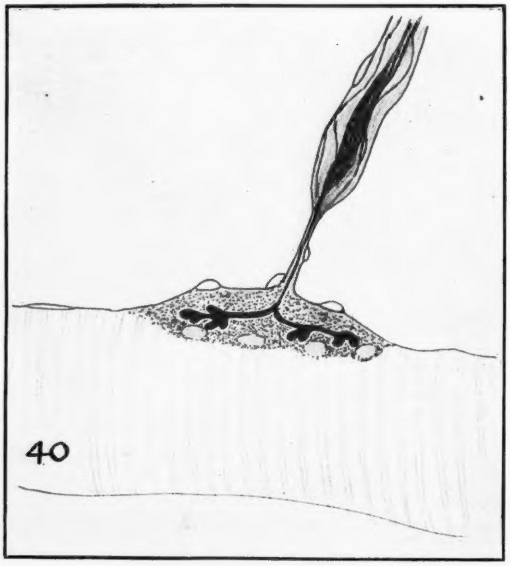

FIGURE XL.

ILLUSTRATIONS TO THE ARTICLE BY DR. HERBERT J. WILKINSON.

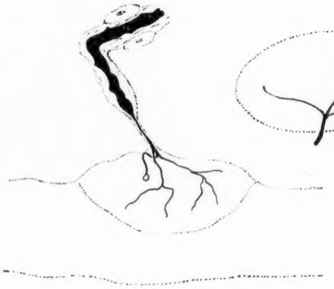

FIGURE XLIA.

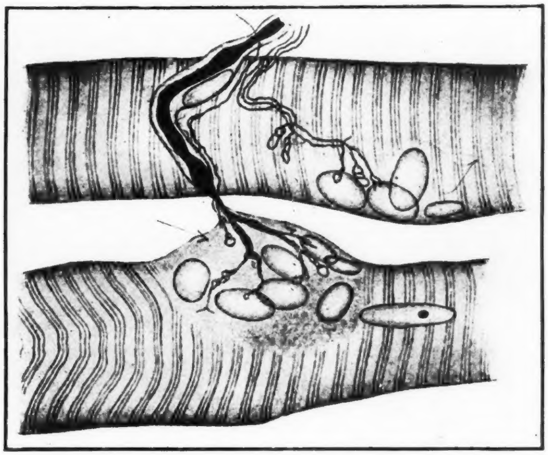

FIGURE XLIB.

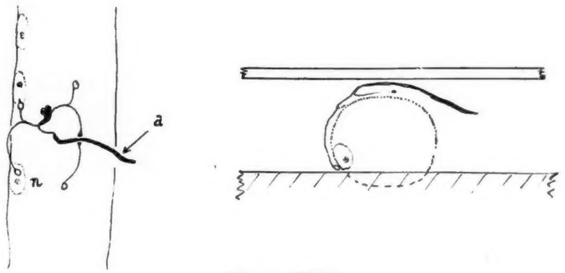

FIGURE XLII.

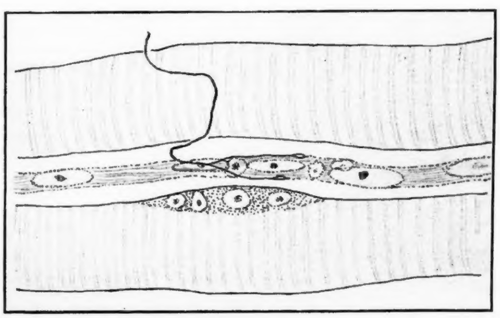

FIGURE XLIIIA.

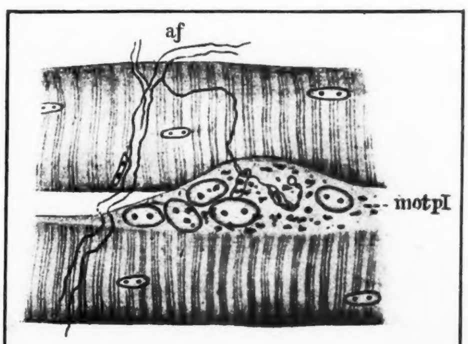

FIGURE XLIIIB.

ILLUSTRATIONS TO THE ARTICLE BY DR. HERBERT J. WILKINSON.

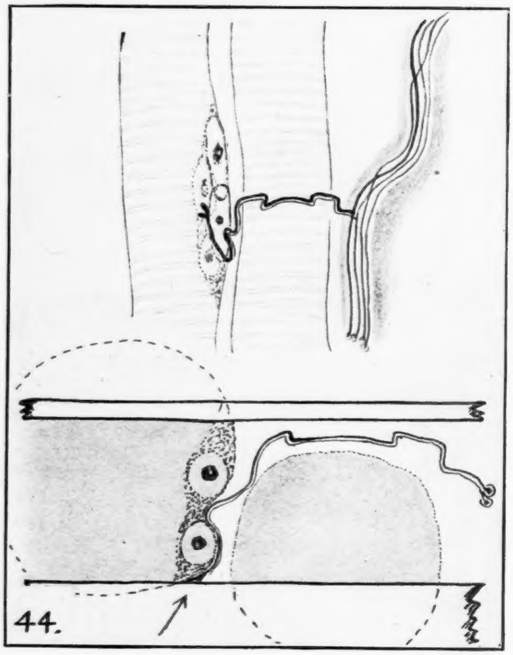

FIGURE XLIVA.

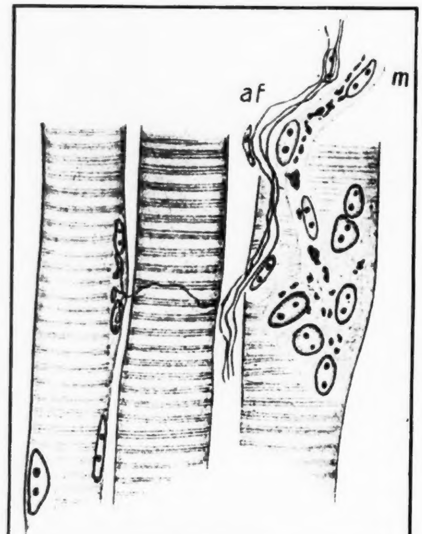

FIGURE XLIVB.

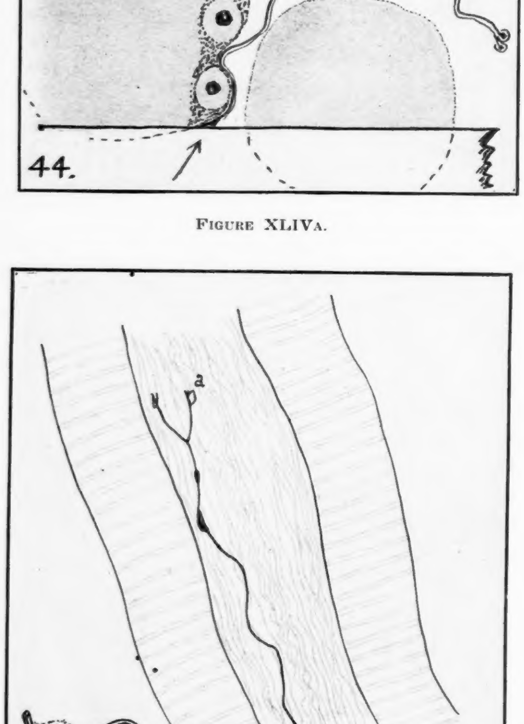

FIGURE XLV.

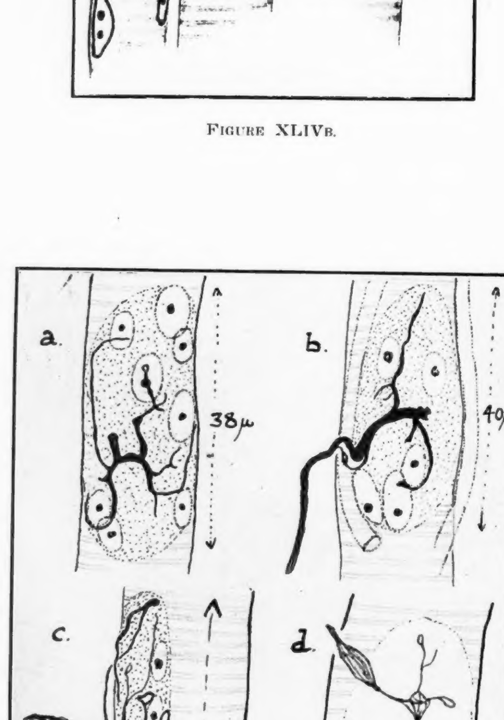

FIGURE XLVI.

of higher metabolic activity, that is, where there is a greater demand for capillaries to provide the raw material for such activity and to remove the waste products that would appear in greater abundance. The sympathetic nerves would then tend to grow up the physiological gradients just as the peripheral ends of sensory nerves do and so it is quite natural that sympathetic endings would sometimes be seen apparently lying in close relation to sole plates. Their function, however, may be concerned only with efficient circulation.

Kuntz[30] who used the silver technique, has also submitted evidence confirming the work of Boeke on the sympathetic innervation of muscle, but his figures are subject to the same criticism. These figures show an unmistakable relation of the sympathetic nerves to the blood vessels and consequently his report cannot be accepted as definite proof of the sympathetic innervation of striated muscle fibres. In the cases in which his figures show sympathetic fibres ending in delicate end nets on muscle fibres, there is not sufficient evidence that they terminate hypolemmally and they can just as readily be interpreted as representing the growing ends of the sympathetic nerves as described above.

It appears to be quite evident, then, that those who have published confirmation of Boeke's work with regard to the occurrence of sympathetic endings in or near sole plates, have not fully considered the possibility of their being sympathetic nerves associated with the vascular channels.

Boeke's Preparations of Accessory Endings in Sole Plates of Somatic Motor Endings.

As an example of an accessory fibre ending in a sole plate, Boeke showed me the preparation from which he drew Figure XV of his 1927 article (Boeke[5]). I found on examining this preparation that it laid itself open to an entirely unexpected interpretation. In this figure (reproduced here in Figure XLIB) Boeke shows an ordinary somatic motor ending in its sole plate on a muscle fibre. In this plate is also shown an ending of a fine non-medullated fibre which he claims is a sympathetic fibre. When this ending is focused and its fibre carefully traced back, it is found to bend back near the surface of the sole plate and to arise as a branch from the somatic motor fibre and is thus really a part of the axonal arborization in the sole plate (see Figure XLIA).

This accessory ending is then in my opinion one of the branches of the motor ending, similar to the branches in the motor plate seen in Figure XVII and other figures in the same article.

The accessory "fibre" shown parallel to the medullated fibre appeared to me to be undoubtedly the outline of the neurolemmal sheath which is somewhat wrinkled.

With regard to the other endings seen in this figure, since they occurred as fragments amongst a mass of rather heavily stained tissue which is not shown in the figure, I could not come to any definite conclusion about them.

Boeke's Evidence of Sympathetic Endings in Experimental Material.

Boeke's main evidence of the sympathetic innervation of striated muscle depends upon his experiment on an extrinsic eye muscle of the cat. In this he cuts the trochlear nerve "as near to the brain stem as possible" and three and a half days afterwards, when the cat died, the *musculus superior obliquus oculi* was stained according to the Bielschowsky technique. After examining the preparation thus made, Boeke reports that all medullated nerves together with their endings, both hypolemmal and epilemmal, had degenerated. He still found, however, many apparently intact non-medullated fibres and hypolemmal endings of non-medullated fibres, all of which he claims must be sympathetic in origin. Before coming to such a conclusion, however, one must first carefully examine all the possibilities.

In an earlier part of this paper reference has already been made to the great number of afferent (sensory) endings which occur in eye muscles. It was there pointed out that these endings mostly occur on non-medullated terminal and collateral branches of medullated nerves. Besides this, even the motor nerves, especially in young animals, are sometimes found to have relatively long non-medullated terminal branches. It is first necessary then to be quite sure that such an experiment as Boeke performed will bring about the disappearance of all these endings. There is evidence, however, that such a conclusion is not justified. First with regard to degeneration time. From observations I have made on Agduhr's preparations and which will be described later, it is quite evident that three and a half days are quite inadequate for the degeneration of non-medullated terminal and collateral branches of somatic nerves. This is substantiated also by the fact that Boeke himself reports that on repeating his experiment and allowing a longer degeneration time, the endings were not so numerous. But even if little endings are found in the superior oblique muscle a month after section of the trochlear nerve, it is not certain that they are of sympathetic origin, because there is a far more serious criticism of this experiment than the one of inadequate degeneration time. The works of Sherrington and Tozer,[31] of Tozer[32] and of Nicholson[33] show that some of the ganglion cells from which the afferent fibres to eye muscles take origin, are in all probability situated in the course of the nerve trunk between the brain stem and the eye muscles, so that all these afferent fibres cannot be thrown into degeneration by cutting the eye muscle nerves near the brain stem. It is true that in the case of the trochlear nerve trunk these ganglion cells do not appear to be so numerous as they are in the trunks of the oculo-motor and the *abducens* nerves, but it is evident that before any definite conclusions can be arrived at with regard to undegenerated endings in the superior oblique muscle after section of the trochlear nerve, the nerve should be cut as far away from the brain stem as possible, before it receives its sympathetic contribution and the distal portion

carefully examined for the existence of ganglion cells. In Boeke's experiments the above precautions were not taken.

In Boeke's preparations, then, in which only three and a half days were allowed for degeneration of the nerve fibres, we may find, first, intact epilemmal afferent endings, secondly, epilemmal afferent endings which are on their way towards degeneration but which can still be detected, and, finally, if the cat is young, perhaps some hypolemmal endings of non-medullated terminal and collateral branches of somatic motor nerves. In the preparations in which longer time has been allowed for degeneration, we may still find intact epilemmal afferent endings, as it is quite possible that some fibres have escaped being cut off from the ganglion cells which exist peripheral to the point of section of the nerve trunk.

But it may be objected that all the endings figured by Boeke are hypolemmal and that the above criticism, as applied to his experiment in which a longer time was allowed for degeneration, does not meet the case. We must then ask what evidence Boeke has put forward in support of his claim that all the endings he figures are really hypolemmal.

One cannot help thinking that many of the endings he figures, bear an unmistakable resemblance to the small afferent endings which are so plentiful in eye muscles. Moreover, all except one figure (Boeke,[5] Figure VI) show that the endings are seen in surface view on the muscle fibres and not in profile or transverse section and it is quite possible that Boeke's interpretation of their hypolemmal position is not correct. The one exception referred to shows an ending in profile, but this occurs in the three and a half days' material and this may be an incompletely degenerated somatic motor ending. Although Boeke claims that he found hypolemmal endings in the experiment in which he left longer time for degeneration after section of the trochlear nerve, he has shown no figures of them, so it is not possible to give an opinion about them.

In support of his conclusions with regard to sympathetic endings in the superior oblique muscle, Boeke cut the sympathetic nerves proceeding from the superior cervical ganglion and was convinced that the number of sympathetic endings in the superior oblique muscle was less. But it seems difficult to imagine what reliable evidence could possibly be obtained in such an experiment, for the number of afferent endings occurring in eye muscles and the possibility of confusion with sympathetic endings, if they really occurred, is so great that it would hardly be possible to notice a decrease in the number of these little sympathetic endings. This would be the case, even if the staining method used was not so fickle and gave perfect results.

It is apparent from what has been said, that evidence of sympathetic innervation of striated muscle fibres, based upon investigation of eye muscles, must be accepted with great caution.

Boeke's Eye Muscle Preparations.

Boeke was able to show me only the preparations taken from the three and a half days' degeneration material, as he no longer had those from material in which a longer time was left for degeneration of the nerves. He claimed that the endings which he showed me, were all hypolemmal endings of sympathetic nerves. I was not convinced, however, that such was the only interpretation that could be put upon them. First, in some cases, by careful focusing the endings appeared to me to be readily excluded out of the muscle fibre and were distinctly epilemmal.

Figure XLII is a sketch of one of these endings as seen under the microscope, together with a reconstruction in the third dimension. The fibre *a* is rather coarse, but no myelin sheath is distinguishable. The ending comes into focus well before the cross striations of the muscle fibre and by the most careful focusing no nucleated protoplasmic sole plate could be detected, although the slide was counter stained with hæmatoxylin in order to show the nuclei. The only nucleus that lay near the ending, was that marked *n*. Other nuclei were present, but lay along the left hand margin of the fibre. The reconstruction reveals the fact that the fibre and ending can be excluded out of the muscle fibre and also that if the ending is to be regarded as hypolemmal, then it would spread almost half way round the muscle fibre. I have never seen an ending, even of a large motor plate, occupying such a large segment of the muscle fibre; the usual is about one-quarter.

The balance of evidence appears to me to be distinctly in favour of its being an epilemmal sensory ending, for the ending is spread out over too large an area, has no nucleated sole plate and can be excluded out of the muscle fibre as shown in the figure and finally also looks remarkably like one of the larger afferent endings so common in eye muscles.

The probability of this interpretation was increased, when on going carefully through one of these sections, I found a medullated nerve which had not degenerated, and also found some other small endings which were undoubtedly epilemmal. It must be pointed out that the presence of only one undegenerated medullated fibre is quite sufficient to account for many such afferent endings, as non-medullated collateral branches are given off so freely and the terminal branches are so numerous.

With regard to other endings shown to me in these eye muscle preparations, I came to the conclusion that Boeke had not sufficiently considered the possibility of their being sympathetic nerves accompanying blood vessels which he does not show in his figures. Take, for instance, Figure XIII of his 1927 article, reproduced here in Figure XLIIIB. This shows a muscle fibre with a very large motor plate in profile and in which occurs the ending of a fine non-medullated nerve fibre. In the original preparation from which the drawing was made,

there is a blood vessel containing blood elements running along between and parallel to the two muscle fibres (see Figure XLIIIA). The motor plate was limited in area to about the space occupied by the three sole plate nuclei which lie closest to the cross striations. The rest of the tissue in this plate lies outside the muscle fibre and belongs in part to the vascular channel before mentioned. The nerve fibre figured lies only in this outside tissue and does not enter into any relation with the motor plate, neither is there any evidence of the existence of an end net, such as is figured at the termination of this fine fibril.

There was doubt about the terminal relations of only one ending that was demonstrated to me. This one is figured by Boeke's 1927 article (Boeke,[5] Figure VI) and is here reproduced in Figure XLIVB. This has already been referred to above, where it was pointed out that, even if it was a hypolemmal ending, the possibility of its being an undegenerated somatic motor ending could not be excluded, as the degeneration time was so short.

In the original preparation the relations of the structures make it appear as if the fibre ends hypolemally, but on careful examination this was not so apparent, for I could find no evidence of the fibril entering into and ending in the sole plate as figured (see Figure XLIVB). Moreover, I could not detect any branches of the ending actually in the sole plate. The fibre approaching the plate is accompanied by another fine fibril not shown in the figure and both arise as collateral branches of larger nerves which appeared to me to show some evidence of being finely medullated. On careful focusing the two fibrils could be traced down through the section and always appeared to be external to the muscle fibres and to be cut off finally at the surface of the section. The fibres may merely be intact afferent fibres, passing between muscle fibres and running close to the sole plate of a degenerated somatic ending.

In Figure XLIVA is a diagrammatic reconstruction of his preparation in the third dimension in which structures are projected on to the one vertical plane.

If the sole plate is that of a degenerated motor fibre, this may have approached the plate in the direction of the arrow and therefore no signs of it are visible in this section. The sections were not serial sections, therefore it was not possible to verify this. Two stained fragments were seen in the sole plate, but I could not link them up with the fibrils in any way and could not be sure that they were not hæmatoxylin stained particles of chromatin in the nuclei. It is seen, then, that it is very difficult to exclude the possibility that this preparation may represent fine afferent fibres passing over a degenerated motor plate. Even if it is a hypolemmal ending, it is not certain that it is a sympathetic ending, because the degeneration time is too short.

In conclusion, then, I wish to state that I was shown no preparation from Boeke's eye muscle material which in my opinion can be accepted as definite evidence of the sympathetic innervation of striated muscle fibres.

Before this question of the innervation of eye muscles is left, reference should be made to an observation recorded by Woollard.[34] He submits a figure of nerve endings which he found in the *musculus superior rectus oculi* of a rabbit. In this he shows an ordinary somatic motor ending on one muscle fibre and a rather elaborate ending of a finer and apparently non-medullated nerve fibre lying in relation to a smaller muscle fibre. In commenting on this he writes:

> If this latter ending is to be regarded as a sympathetic ending, then the distribution of the two kinds of nerve fibres in ocular muscles agrees with Kulchitsky's and not with the Boeke conception.

This elaborate spray looks like a typical afferent one and no doubt if its fibre could have been traced back, it would have been seen to arise eventually from a medullated nerve.

After duly considering, then, all the possible sources of fallacy in experiments conducted on eye muscles and also after a critical examination of the original preparations, reproductions of which Boeke has submitted as evidence of the existence in eye muscles of a sympathetic innervation of striated muscle fibres, I remain entirely unconvinced.

Boeke, however, in conjunction with Dusser de Barenne,[35] has submitted further evidence based on a degeneration experiment on intercostal muscles and this has appeared more convincing and has probably done more to convert the sceptical and to establish his hypothesis than Boeke's own earlier works.

Evidence of Sympathetic Endings in Intercostal Muscles.

Boeke and Barenne cut the sixth, seventh, eighth and ninth thoracic nerve roots beyond the spinal ganglion and, after leaving a month for degeneration of somatic nerves, examined intercostal muscle preparations and reported the existence of undegenerated hypolemmal endings of non-medullated nerve fibrils which they claim are of sympathetic origin.

An inspection of the figures they submit, however, shows some nerve fibres which may be sympathetic nerve fibres, associated with vascular channels, while the more elaborate endings are very suggestive of little terminal sprays of sensory endings. Even these may be vascular nerves and the suggestion put forward by Hinsey,[36] that they may be regenerating fibres, must also be considered. The authors claim, however, that the endings figured are all hypolemmal and if this claim can be definitely substantiated, then they have a strong case; but there is no certain evidence that these fibres are hypolemmal, as they are seen only in surface view and not in cross section. Reference, too, has already been made above to the fact that sensory nerves under the pleura may represent a source of fallacy in these experiments. To this must be added the fact that:

A few of the cells of the spinal ganglion usually lie outside the naked eye limits of the ganglion even to a millimetre or so beyond (*i.e.* distal to) the point at which the primary dorsal division of the nerve is given off (Sherrington,[37] page 222).

Boeke and Barenne give no evidence that they were aware of this fact, so the possibility that some of the endings they figure may be afferent (sensory) endings cannot be overlooked. It is true that they claim that all medullated nerve fibres had disappeared, but this does not exclude the possibility of non-medullated afferent nerve fibres with their endings remaining intact, for Ranson[38] has shown that a proportion of the sensory fibres entering by the posterior root is associated with the smaller ganglion cells and is non-medullated. The evidence submitted by Boeke and Barenne then rests on the rather inconclusive proof of the hypolemmal position of the endings they figure, and in such cases the subjective factor entering into the observations cannot be regarded as inconsiderable.

I was, however, shown their original preparations and found that they were capable of yet another interpretation.

The Preparations of Boeke and Barenne.

I was very disappointed in the preparations of Boeke and Barenne, for in one case the "endings" were in no relation whatsoever to muscle fibres, but lay in a mass of connective tissue (see Figure XLV). Also the fibres appeared to be cut off at the upper and lower surfaces of the section, after pursuing a very oblique course through the section. The endings were not true end reticula, but varicosities in the fibrils, the fibrils being cut at the surface of the section just beyond a varicosity. The "endings" were thus artificial endings. In no case had I the least suspicion that the "endings" could be interpreted as being true hypolemmal end reticula in muscle fibres.

I did not see the preparation which is reproduced in Figure II of their article (also reproduced in Boeke's 1927 article, Figure XXXVII), as Boeke said that it was no longer good, so I am not able to give my impression of it.

In view of the criticism of this work mentioned in the last section, I wish to state that the precautions necessary to bring about degeneration of all afferent nerves were not taken, as they were not aware of the existence of ganglion cells lying so far peripherally from the spinal ganglion as described by Sherrington. To meet all these criticisms and at the same time to try to confirm their previous work, Boeke and Barenne are repeating the experiment.

Evidence of Sympathetic Endings in Extremity Muscles.

Apart from the work done in Boeke's laboratory, probably the most important confirmatory evidence of the sympathetic innervation of striated muscle fibres is that put forward by Agduhr[28] who conducted degeneration experiments on the extremity muscles of cats.

Agduhr cut the roots of all spinal nerves which enter into the formation of the *plexus brachialis* of a cat, namely the fifth, sixth, seventh and eighth cervical and the first and second thoracic. Each root was cut "immediately before the outer aperture to or in the *foramen intervertebrale*, giving careful attention not to damage the grey *ramus communicans*." Five to six days were allowed for degeneration of the nerves, after which time Agduhr found that preparations of interosseous and lumbrical muscles of the anterior extremity contained undegenerated endings on the muscle fibres. He concluded that these must be of sympathetic origin. Some of these endings, he claims, are hypolemmal and are therefore sympathetic efferent endings, while others, however, he thought were epilemmal and concludes that they are sympathetic afferent endings. Agduhr claims that he obtained similar results when he left forty-five days for degeneration of somatic nerves, for in a footnote he states that he carried out a set of experiments with a degeneration time of forty-five days and that "the results were exactly identical. Both hypolemmal and epilemmal intact nerve endings were found, the former in much larger number than the latter."

Some of the nerve fibres which Agduhr figures, look very much like sympathetic nerves on blood vessels (see Figures I, III and VIII of his article). The larger endings, however, shown in Figures III, IV, V, VI and VII, are described by him as "big plates of transition form between the ordinary type of sympathetic and motor plates" and others again (in Figures X and XI) which he regards as sympathetic sensory endings, make one doubt whether all the somatic nerves had been thrown into degeneration. This conclusion is based on the fact that I have carefully examined several interosseous and lumbrical muscles from cats and rabbits and also from human material and have never seen endings such as Agduhr figures, except those which were undoubtedly somatic motor endings or endings on muscle spindles. If such large endings of unmyelinated nerves occur in these muscles and so frequently as Agduhr would lead one to suppose, it would be almost impossible to miss them.

Agduhr's Preparations.

As mentioned above, I was also given the opportunity of spending some time in the laboratory of Professor Agduhr, in Upsala, Sweden. After demonstrating his preparations to me, Agduhr generously left his slides in my possession during the whole of my stay with him, so that I was able to make a very thorough examination of them. He also put at my disposal for purposes of comparison some preparations containing normal tissue which had been stained in the same way and about the same time.

Some of the endings demonstrated to me were undoubtedly hypolemmal (see Figure XLVI), but I eventually concluded that they were probably undegenerated somatic motor plates and for the following reasons. First, the endings were similar in size and structure to normal somatic plates, also they were endings of coarse fibres which looked as if they were medullated and, finally, Agduhr's

technique in these preparations fails to demonstrate the sympathetic nerves on blood vessels.

With regard to the size and structure of these endings, I carefully measured all that I could find in the preparation and found that in every case they fell well within the limits of ordinary somatic motor endings. Measurements were made of twenty-four normal motor plates in similar material and these were found to vary in length from 35 μ to 45 μ, the average being 36 μ. The lengths of the undegenerated plates in Agduhr's experimental material varied from 33 μ to 40 μ (average 38 μ). in no case did I find any fine varicose nerve fibrils nor did I find any small endings which were not fragments of large plates. Fortunately the sections were mounted in serial order, so it was possible to trace the fibres from section to section and to reconstruct the complete endings from fragments found in consecutive sections.

With regard to the endings which Agduhr reproduces in Figures XII, XIII, XIV, XV, XVI and XVII of his article and which he thinks are epilemmal afferent sympathetic endings, I found that they all occurred in one large muscle spindle. On careful examination of the series of sections in which the spindle occurred, it was seen that the large nerve fibre leaving the spindle was affected by a gradually increasing degree of degeneration as it was traced away from the spindle. Near the equator of the spindle, where the fibre began to divide into its terminal arborization, the neurofibrillar structure of the axone was still distinguishable and in relation to the intrafusal fibres not only at the equator of the spindle, but also towards the distal ends similar numerous fine fibres were seen, such as Agduhr figures. As to the relation of these fibrils to the sarcolemma, they appeared to be distinctly epilemmal and in my opinion there seemed to be little doubt that they were incompletely degenerated epilemmal somatic afferent endings of the spindle. In another spindle examined in the same series the same thing was seen. A tendon spindle was also seen which had fine branches ending in end nets. The complete arborization in this tendon spindle seemed practically intact, but in its fibre increasing degrees of degeneration were seen as it was traced away from the spindle. This fibre was seen to join eventually the same bundle of nerve fibres as the fibre which supplied the large muscle spindle first mentioned.

A further example of incompletely degenerated muscle spindle endings was observed in the series of sections from the five days' degeneration material. Here again the terminal arborization of the somatic afferent fibre seemed intact, although the fibre of supply showed increasing signs of degeneration as it was traced away from the spindle.

These facts are quite sufficient evidence that five or six days are insufficient to cause complete degeneration of non-medullated terminal branches of somatic nerves and therefore offer strong support to my criticism of Boeke's eye muscle experiments mentioned previously.

With regard to Figures X and XI of Agduhr's article,[(28)] these occurred in sections of a lumbrical muscle and resembled somatic sensory endings I have seen in this muscle. These endings lay in connective tissue and were quite large in one case, Figure XI being 45 μ and in the other, Figure X, being 66 μ in length. In both cases the endings were of what appeared to me to be undoubtedly coarse medullated nerve fibres.[1]

Conclusion.

It is seen, then, that after a careful and long continued search through a wide range of material and after a critical examination of some of the original preparations reproductions of which have been published as evidence of the sympathetic innervation of striated muscle fibres, I cannot but adopt a sceptical attitude towards the whole question and conclude that it is very doubtful whether any histological evidence of a direct innervation of striated muscle fibres by sympathetic nerves exists.

Some Physiological Considerations.

Before this subject of the sympathetic innervation of striated muscle fibres is left, it would not be out of place to refer briefly to some physiological aspects of the problem. First, with regard to the effects produced by cutting sympathetic nerves. The principal effects produced, for example, in a limb, are slight increase in volume and temperature, sometimes loss of tone and also a greater susceptibility to fatigue. (See also Popa.[(39)]) It appears that all these effects can be explained by regarding them as changes produced in the control of the circulation. In a normal muscle there is a delicate but perfect adjustment between muscle activity and blood supply and any factor which interferes and upsets this balance, will eventually result in malfunction. The muscle fibres are under the direct influence of the anterior cornual cells of the grey matter of the spinal cord and they in their turn are under the influence of higher centres at different levels in the brain stem and cortex. Similarly, the blood vessels are also under the influence of a hierarchy of centres. This is on the efferent side of the nervous system, but all these centres, both in the somatic and in the sympathetic arcs, are under the influence of afferent neurones. It is quite possible also that the descending tracts in the somatic arcs control the hierarchy of efferent centres in the sympathetic arcs, so that complete and perfect adjustment of blood supply to muscle activity can be maintained.

Muscle tone is probably maintained through the influence of lower brain centres acting through the anterior cornual cells under the controlling influence of the cortical (pyramidal) cells. When through disease any of the infracortical centres function

[1] The cats used in these experiments were not only young—they were only four months old—but they were really not quite normal for their anterior extremities had been abnormally developed by an interesting course of training, in experiments which had been devised to ascertain whether any post-natal growth could be detected in the spinal ganglia and spinal nerves (Agduhr[(28)]).

abnormally or cease to function, then definite signs appear in the muscles. Also, when the cortical influence is removed through damage to the pyramidal (cortico-spinal) tract there is an alteration in the tone of the muscles affected. Again, even when the hierarchy of somatic arcs is intact, muscle is very sensitive to alteration in the blood supply. It is beyond the scope of this article to enter into the complete discussion of muscle tone, but it does not appear inappropriate to point out that there appears to be quite an adequate and delicate mechanism for the maintenance of muscle tone without the necessity of a direct control through the sympathetic system.

With regard to the control of the circulation, besides the existence of a central control, there is evidence that there is a peripheral mechanism for compensation and readjustment when the sympathetic nerves have been cut (Starling[40]). A consideration of this question is wrapped up in that of the way in which the blood vessels function. It seems strange that no one has seriously considered the possibility of the blood being hurried through the arterioles by waves of contraction which pass along their walls. In other parts of the body where plain muscle tissue occurs, it is found to have the inherent quality of rhythmic contraction and that this activity can be influenced and controlled through the nervous system. If we assume that this is what occurs in blood vessels, it appears easy to explain, for example, the mechanism of vaso-dilatation. Starling makes reference to the work of Bowditch and Warren who showed the effect on the volume of hind limbs of the cat of stimulating the sciatic nerve with conduction shocks at different rates. With one shock per second there is considerable dilatation, whereas with sixty-four shocks per second there is vaso-constriction. This can be explained by assuming that the less frequent stimulations cause waves of contraction to pass down the walls of the muscular arterioles, forcing along the blood and opening up a wider capillary bed, while more frequent stimulation throws the walls of the arterioles into a state of tonic spasm and prevents or decreases the flow of blood into the capillaries with consequent decrease of intra-capillary pressure and collapse of the capillaries.

Returning to the consideration of a peripheral mechanism for readjustment, it can be shown that the blood vessels are not only under the influence of the post-ganglionic sympathetic vasomotor nerves, but stimulation of sensory nerves can give rise to vaso-dilatation which means according to the above view capillary engorgement. This is brought about through collaterals of sensory nerves which end in relation to blood vessels. There is histological evidence of this, as we have preparations which show medullated nerves passing to blood vessels and finally breaking up into fine non-medullated fibres which become lost in the plexus of nerves around the blood vessels. Woollard[41] has also submitted evidence of this. But how do these nerves act? It is said that the one set of nerves, vaso-constrictor, causes vaso-constriction and another set, vaso-dilators, causes dilatation, but it is difficult to understand from morphological evidence how these results could be brought about, unless a double innervation of the contractile cells of the vessels is postulated. But there is no evidence of this and in our opinion such a mechanism is unnecessary. On the view put forward here stimulation of sensory nerves causes rhythmic contraction of the vessel walls and this leads to capillary engorgement or vaso-dilatation. Over stimulation of the sensory endings can also lead to vaso-constriction, as is seen in the action of certain irritants applied to the skin which result in vaso-constriction and a sense of cold.

An interesting case of the effect on the circulation of over stimulation of sensory nerves is that seen in certain chronic varicose ulcers. Corlette[42] describes varicose ulcers which would not heal, but often did so when the sensory nerves of the part were cut to relieve the patient of the pain. If the view put forward above is correct, then the excessive stimulation of sensory nerves prevented healing of the ulcer by interfering with the circulation. As soon as the sensory nerves were cut and the peripheral ends degenerated, spasm of the arterioles was released and the circulation was restored, so that the conditions of the circulation necessary to promote healing were reestablished.

Besides these purely nervous mechanisms for the control of the circulation, there is a chemical one. With regard to this chemical influence, this not only includes that of the endocrines, but there is evidence that products of metabolism directly affect the blood vessels.

There are thus seen to be many factors concerned in the flow of blood through the peripheral vessels, leading to the maintenance of efficient circulation in a working part and it follows that proper coordination and adjustment of all these mechanisms are necessary to the proper and normal functioning of that part.

Under normal conditions, when motor neurones are stimulated, appropriate sympathetic neurones are also stimulated so that blood is hurried through the vessels. The fact that fatigue occurs in a structure whose sympathetic nerves have been cut, clearly shows that their presence is probably necessary in order to prevent it and their presence is able to prevent fatigue mainly because impulses through them actively maintain an efficient circulation by causing a more rapid flow of blood through the small muscle walled arteries and consequent dilatation and widening of the capillary bed.

The first effects produced, then, by cutting the sympathetic nerves are due to the removal of the central control of the circulation. The vessel walls are paralysed and dilate under the influence of the general blood pressure. This leads to engorgement of the vessels, increased volume of the limb and a rise in temperature and as the circulation under

these conditions is not normal, there may be a decrease in the tone of the limb. After a time the plain muscle cell of the vascular walls may recover to some extent from the initial shock and may lead to the reestablishment of conditions towards the normal by continuing to contract rhythmically, uninfluenced by nervous control. Starling states that a compensation may be established within a few days.

Again, there are the effects produced by experimental stimulation of the sympathetic nerves. For a summary of the effects produced first, see Popa[39] who describes results produced not only by electrical stimulation, but also in pharmacological and serological experiments. Popa states that the general effect of stimulation of the sympathetic nerves is analogous to the drifting of the calcium-potassium balance in the direction of calcium and the stimulation of somatic nerves to shifting in the direction of potassium. Also he describes the production and effects of what he calls somatic serum and sympathetic serum. Such results as he describes, seem capable of explanation without the necessity of postulating the existence of a direct sympathetic supply to muscle fibres. It is quite possible that the metabolism of striated muscle and of plain muscle tissues respectively may result in the formation of different metabolites which have a stimulating effect on the other. For example the products of metabolism of the plain muscle of the vascular channels might act as a stimulus to striated muscle tissue and *vice versa*, or again the metabolites due to the activity of the one may tend to neutralize or facilitate the removal of the metabolites due to the activity of the other. Popa's experiments also were done on pigeon's wings and it is quite possible that here the tissues are more sensitive to these products and there may be a very delicate balance between the two tissues.

Orbeli, quoted by Fulton,[44] also describes the effects of stimulation of the sympathetic. Fulton states (page 409) that:

> Orbeli delivered to an excised muscle repetitive twitches at short intervals, and when fatigue had commenced to show itself by a diminution in height in successive twitches, the sympathetic was stimulated and after a considerable latency the twitches became augmented, the height of the effect occurring some time after sympathetic stimulation had ceased. Secondary circulatory alteration can be excluded, since isolated muscles were utilized.

If, as mentioned above, activity of the plain muscle in the walls of the blood vessels produced substances to which striated muscle was sensitive or which facilitates the removal of metabolites due to striated muscle activity, then the results produced in Orbeli's experiments would be just what would be expected.

Gaissinsky and Lewantowsky[43] give an account of changes produced in striated muscle after sympathectomy. They say that the histological changes are degenerative and do not seem to be dependent on changes in the vascular supply, but they do not state how they come to this conclusion.

The view put forward in this paper, then, with regard to the sympathetic innervation of striated muscle is that sympathetic nerves are concerned only with the regulation of the blood vessels and do not act as direct sympathetic efferent nerves to muscle fibres. The amount of blood and the rapidity of the circulation of blood in the capillary bed depend upon the amount passed on by the small arteries and the amount drawn off by the smaller veins which are also muscular. Tone in muscle and the general trophic state of muscle are maintained by a definite coordination between muscle activity and the mechanism which is concerned with the removal of products of metabolism, the former being under the influence of the somatic nerves and the latter being under that of the sympathetic, while both are under the influence of an elaborate afferent mechanism.

The Plurisegmental Innervation of Muscle Fibres.

With regard to this question of the plurisegmental innervation of individual muscle fibres, investigators up to the present have looked for evidence of the existence of a single muscle fibre, of two motor end organs, associated with two motor nerve fibres which arise from cells in two different segments of the cord. Fulton[44] gives a summary of the work done in this field, both anatomical and physiological, and reproduces two diagrams of Lederer and Lemberger in which they show two possibilities with regard to the plurisegmental innervation of individual muscle fibres. Such suggestions as they put forward, however, rest upon a rather frail foundation of histological fact, in spite of the work of Agduhr[45] and Garven,[12] for muscle fibres with two end plates have not been shown to be of very frequent occurrence.

During the present investigation I have kept a constant lookout for the occurrence of two plates on one and the same muscle fibre and have found that, whereas in the frog and salamander I have sometimes seen examples of this, such an occurrence has never been observed in any of the muscles examined in higher animals. The endings seen in frog and salamander muscle tissue, however, were always of the immature type such as were described above and in no case have I observed more than one mature motor ending with its fucoid fronds lying in relation to a muscle fibre.

Agduhr reports that he has frequently seen two mature plates lying close together on muscle fibres in the interosseous and other muscles of a cat and claims to have proved by differential degeneration experiments that they were derived from different segments of the cord. I kept a special look-out, therefore, when examining interosseous muscles, but never succeeded in finding one, in spite of the fact that the gold technique offers special facilities for obtaining satisfactory evidence on this point, for, if there is the slightest suggestion that in a preparation two plates appear to occur on the one fibre, the fibres can be completely separated from one another so as definitely to settle this point.

Garven,[12] also working with the gold technique, could not find two plates on the short muscle fibres of the smaller muscles, but did succeed in finding examples, but only two, of the existence of two plates on very long fibres found in the *panniculus carnosus* of the hedgehog, but here they were found very far apart and at the ends of the muscle fibres examined, quite a different thing from what Agduhr figures.

While with Agduhr, I examined the silver preparations which he figures in his article. The material was taken from cats in which spinal nerves had been cut at different times, namely, the seventh cervical ninety-six hours and the eighth cervical sixty-eight hours before the animal was killed. On examining silver perparations of the interosseous muscles supplied from these segments, Agduhr found that some nerve fibres and their plates had degenerated and others were sound. Further, he also claims to have found, lying close together on one and the same muscle fibre, both a sound plate and a degenerated one, thus demonstrating the occurrence on one muscle fibre of two plates which are derived from fibres arising in different segments of the cord.

The first preparation examined was the one from which Figure III of his article is reproduced. On careful focusing and reconstructing this field in the third dimension, it was possible to show that there were parts of two fibres in the thickness of the section and it was impossible to exclude the possibility that the degenerated plate belonged to the upper fibre and the sound plate to the lower fibre. This conclusion was further substantiated by the following facts. First, the degenerated plate was in a plane about two to three μ above that of the sound plate, secondly, the upper fibre was paler and less distinctly stained than the lower fibre whose granules and striations, on the other hand, were very sharply stained and, finally, a capillary lay in a plane intermediate between those of the two plates. Figure XLVII then represents the above interpretation of the field. *A* and *B* are the two plates and *C* the section of the capillary which lies between the two fibres and between the two plates.

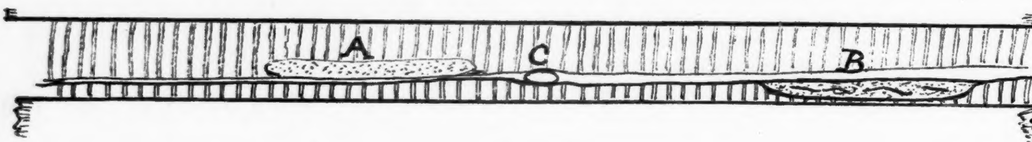

FIGURE XLVII.

Again, Figure I of Agduhr's article contains two plates, one degenerated and one sound, lying "in profile" in relation to a single muscle fibre. Careful measurements of the fibres, however, not only in the horizontal plane, but also in the thickness of the section and a reconstruction of the field in the third dimension showed conclusively the existence of two fibres. If the plates shown in Agduhr's figure are projected on the same vertical plane the diagram seen in Figure XLVIII shows what is obtained.

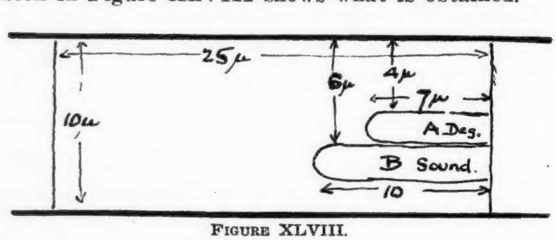

FIGURE XLVIII.

Cross striations could be focused above the plate and below the plate. Measurements in the horizontal plane show that the muscle fibres were 25 μ in diameter; plate *A* was 8 μ and plate *B* 10 μ in width. These measurements reveal the fact that if the muscle tissue seen in the microscopical field and represented in Agduhr's figure was one fibre, then we would have the two plates lying with their planes running into the substance of the fibre towards its centre instead of lying tangential to its surface. The only possible interpretation seems to be that set out in Figure XLIX.

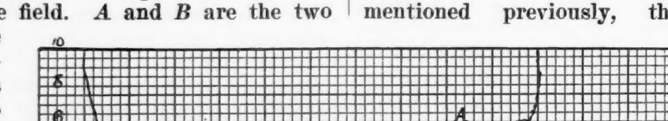

FIGURE XLIX.

In addition to the above facts the same staining reactions were noticed here as in the last case, namely, that the muscle tissue in the upper part of the section was less distinctly stained than that in the lower part.

Several other examples were shown to me, but they invariably admitted of a similar interpretation.

As further justification for the adoption of a sceptical attitude towards the occurrence of two plates lying close together on one and the same muscle fibre, while at Upsala, I repeated my investigation on the interosseous muscle of a cat. As mentioned previously, the gold method is undoubtedly the method *par excellence* for demonstrating the occurrence of doubly innervated muscle fibres if they really existed. Two interosseous muscles were teased from end to end and pieces of tissue from

different parts of two others were carefully examined and not one doubly innervated fibre was found. If there was the slightest indication that two plates belonged to one muscle fibre, the muscle fibres were completely separated. It was estimated that in the interosseous muscles of a cat there are upwards of 70,000 muscle fibres and if the doubly innervated fibres existed to the extent of only 1%, there would be more than 700 of them in each muscle and it would be almost impossible to miss seeing at least one.

The only clearly proved cases of doubly innervated muscle fibres are the two seen by Garven. These were two long fibres, however, and passed through the territory of distribution of two or more spinal nerves and in these cases the plates were found at situations far removed from one another at the ends of the muscle fibres.

Although two mature plates were never seen to occur on one and the same muscle fibre, yet observations made in this present investigation and recorded above seemed to suggest another possibility with regard to the plurisegmental control of muscles.

In the section on *terminaisons en grappes* it was mentioned that immature motor endings in lizard muscle sometimes received contributions from two or more different motor fibres (Figure XIII). It must be emphasized that this condition was quite common in lizard muscle, wherever the immature forms obtain, and undoubtedly represents a common mode of development of motor plates. On thinking over these observations, I was eventually faced by the question as to whether similar observations had ever been made on embryonic muscle and in muscle obtained in nerve regeneration experiments. And this was found to be the case. First, Tello[46] in his work on the development of motor and sensory endings supplies similar evidence (Figure XXXVI) in embryonic material. Also Boeke[5] shows striking examples in his Figures XXVI and XXVII. Again, while I was in Upsala, Agduhr kindly put at my disposal sections of an eight day old mouse stained according to the Bielschowsky technique, and on examining this I found a further example. With regard to similar evidence in degeneration experiments, Boeke[3] has recorded similar observations and when I discussed this with him personally, I found that he had often noticed it.

Now when the stages in the development of immature plates are examined, one must arrive at the conclusion that the collecting together of the non-medullated fibres which contribute to the formation of a motor plate, must result by progressive medullation in a plexus formation. This is shown diagrammatically in Figures L and LI.

Growth of the tissues with consequent elongation of the fibres makes it difficult to recognize the existence of this plexus in adult tissue.

If the above interpretation is correct, then it appears that fibres which enter a muscle, form a plexus from which arise the nerve fibres which

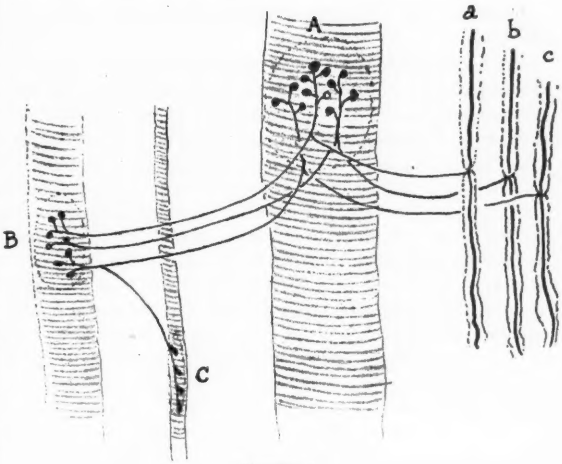

FIGURE L.

terminate on the muscle fibres. It cannot be assumed that the occurrence in muscle of such a nerve plexus brings about a complete fusion of the segmental nerves which supply the muscle, but that it occurs to some extent at least seems highly probable. But even where a muscle receives nerve fibres from only one segmental nerve, it may still come under the influence of more than one segment, because Agduhr[47] has shown by the method of Nissl that the motor fibres of a spinal nerve not only come from the anterior cornual cells of the same segment of the cord from which it arises, but also from similar cells in higher segments.

The above facts tend to show that nervous impulses coming from different segments of the cord are discharged into an intramuscular nerve plexus out of which they pass to individual muscle fibres.

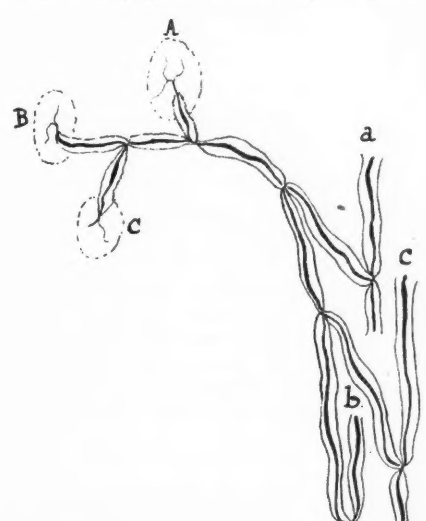

FIGURE LI.

Figure LII shows diagrammatically what is implied.

Such a structure would provide a very efficient mechanism not only for prolonged activity, but for the prolonged maintenance of definite postures, for the work of discharging impulses into the plexus may be taken on by nerve cells of a particular group in rotation. It appears that so long as there is an efficient mechanism for the removal of products of metabolism *et cetera* in muscle tissue, fatigue does not set in very rapidly. Now, in muscle tissue which is a contractile tissue, products of metabolism can be quickly removed and replaced, but in the nervous system the efficiency of the circulation depends entirely on the circulation system itself, so that it

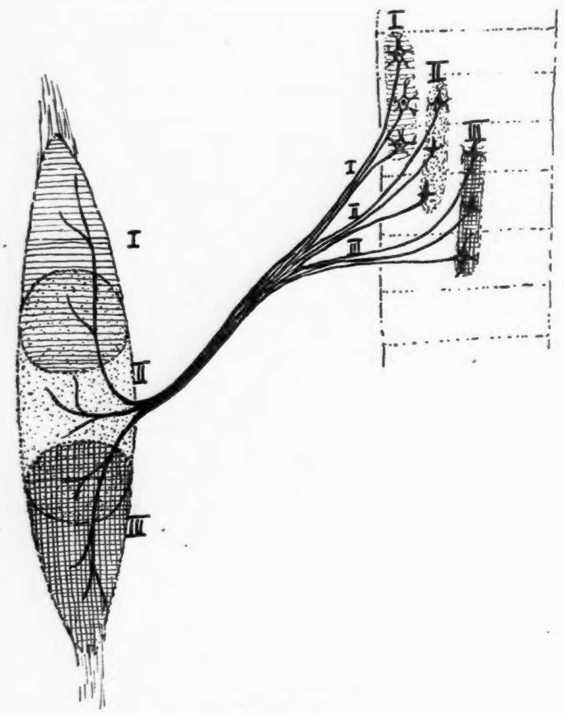

FIGURE LII.

is quite possible that a motor nerve cell is more rapidly fatigued than the group of muscle fibres with which it is physiologically connected. If this is so, then such a mechanism described above would provide a means by which the work of fatigued neurones is taken up by other neurones, for example, in the case of skilled movements or usual postures there is a rhythmic activity in a group of neurones which tends to permit of a more prolonged activity.

Remarks on the Innervation of Muscle Spindles.

During the course of this investigation many observations were made on muscle spindles, as these structures were obtained in the muscles of most of the animals examined. It is beyond the scope of this paper to write a complete account of the comparative morphology of muscle spindles, but as there is still doubt on certain points relating to the innervation of these interesting structures, it is desirable to record those observations which will help to clear up this matter.

Cuajunco[48] gives a very good review of the literature on this subject up to date, so it is unnecessary to lengthen this communication unduly by repeating it. He has, however, omitted reference to the findings of one or two of the earlier workers, particularly those of Perroncito,[14][15] many of whose observations I have been able to confirm, and which have not been generally appreciated in English and American schools.

With regard to the sensory innervation, there appears to be little doubt. Most of the observations of the various workers with regard to the point of entrance, modes of termination of the fibres and relation to the muscle fibres were confirmed. We can find, however, no suggestion as to the significance of the various types of sensory endings. There also seems to be some doubt about the existence of a motor innervation of intrafusal fibres. Herscher (1888) and Huber and de Witt (1897)[49] showed motor endings, so also did Perroncito (1902), but according to Cuajunco, Sherrington denied their presence and Batten and many others were unable to find them. Cuajunco also does not seem to come to any definite conclusions with regard to this important question. I shall, therefore, submit evidence which shows definitely that intrafusal fibres receive motor innervation. In my teased material, prepared by the gold technique, I sometimes obtained spindles with their complete innervation, but besides these there were seen many spindles which were incompletely stained, but which showed sufficient to support the general conclusions. The first spindle which showed unmistakable evidence of a motor innervation, was seen in the intercostal muscle of a lizard (*Tiliqua scincoides*). This is drawn in Figure IX. This figure depicts an intrafusal fibre with its motor ending, that is derived from a motor nerve fibre which is seen to terminate in relation to an extrafusal fibre in the ordinary *terminaisons en plaque*. Another observation of the same kind is recorded in Figure XXIX. In this case, however, the senesory ending is several fields removed from the one photographed. Other statements were mentioned above in the account of *terminaisons en grappes* in reptiles and need not be repeated here. Similar observations were made in mammals and a unique preparation is shown in Figures XXVII and XXVIII, obtained from the *musculus panniculus carnosus* of the spiny anteater (echidna). These figures show a complete spindle with its complete sensory (Figure XXVII) and complete motor (Figure XXVIII) innervation. A bundle of fibres enters the field to the right in Figure XXVIII. It is in a plane somewhat below that figured, and is therefore out of focus. The blood vessel accompanying it, however, is seen. Before reaching the spindle, branches from this bundle end in ordinary motor plates on the ordinary extrafusal muscle

fibre and on reaching the spindle branches terminate in plates on the intrafusal fibres. There is no doubt that the plates are motor, as they occur on collaterals of fibres which end on the extrafusal fibres just as illustrated in Figure IX. Some distance from the spindle a large medullated nerve leaves the bundle of motor fibres and crosses the spindle in the region between the points marked "M" and "S" in Figure XXVIII. This fibre is shown in Figure XXVIII coming into focus just to the right of the letter "S." It then turns back and approaches the spindle from the left in Figure XXVII.

Just before entering the capsule of the spindle, the sensory fibre branches at nodes so that four medullated fibres enter the capsule and terminate in relation to the intrafusal fibres in the typical annulo-spiral endings. The annulo-spiral endings develope on the collaterals arising at nodes of the medullated fibres, as these latter pass parallel to the intrafusal fibres. As the medullated fibres pass away from their point of entrance into the spindle, these endings of these terminal collaterals manifest decreasing development of the annulo-spiral endings, until they appear as *terminaisons en grappes* and the end of the medullated fibre itself ends in one or more beads or grape-like shaped bodies. No other fibres whatever enter the spindle with the sensory nerve. The fine lines seen in the figure are deposits of gold in the neurolemma sheath (see Figure V) of a typical medullated nerve and in the white fibres which belong to the capsule of the spindle.

Elsewhere reference was made to sensory endings in the muscle spindles of the lower vertebrates and it was seen that they first appeared as *terminaisons en grappes* which gradually developed into the more elaborate forms. The structure of the sensory endings in this echidna spindle illustrates the same principle and is further evidence of the grape-like structure of immature endings in general.

With regard to the sympathetic fibres, only those were seen which show unmistakable connexion with the blood vessels in relation to the spindles. This applies to all spindles. Figure XXXIII of a frog's spindle shows this relation very well. The blood vessel in the spindle has not shown up very clearly, but it comes slightly into focus just below the sympathetic fibre near the point of the arrow. Many of the finer nerves described by Cuajunco are undoubtedly those described above as lying in relation to blood vessels and capillaries in the capsule and also in relation to capillaries between the intrafusal fibres. But Cuajunco describes others which enter with the main sensory nerves, and whose fine terminal branches anastomose with the fine branches of the sensory nerve in the developing spindle. The fact that this anastomosis was observed should be quite sufficient to identify the common origin of the fibres. Moreover, observations on immature forms of endings, both motor and sensory, and observations on mature spindles in full grown mammals show that progressive myelination of the sensory fibres usually proceeds to complete subsuming of all these fibrils into one or two large medullated nerves.

Observations on preparations of tissue from lower forms and especially from the salamander, demonstrate the frequency with which non-medullated collaterals can arise from medullated nerves to end in immature forms of endings. Cuajunco is also inclined to accept Kulchitsky's evidence of the sympathetic innervation of intrafusal fibres, but we have shown that the "sympathetic" endings described by Kulchitsky are the motor plates derived from motor fibres as in Figure IX.

We have come to the conclusion that there is no more evidence for the sympathetic innervation of intrafusal fibres of muscle spindles than there is for the sympathetic innervation of muscle fibres. All the preparations examined showed only the sympathetic nerves on the blood vessels.

With regard to the plurisegmental innervation of muscle spindles, evidence of which has been put forward by Agduhr,[46] I was shown the original preparations from which the figures were reproduced, and came to the conclusion that the degenerated endings which Agduhr regarded as degenerated sensory endings, were in one case most probably the degenerated motor endings and in the other were a part of the sensory ending all of which had not degenerated, although its fibre of supply showed increasing signs of degeneration as it was traced away from the spindle.

Summary.

1. All muscle fibres are innervated solely by somatic nerves, that is, cerebro-spinal nerves. Hunter's hypothesis based on the work of Kulchitsky is therefore untenable.
2. *Terminaisons en grappes* that occur in lower vertebrates, may be either (i) "immature" forms of motor terminations or (ii) afferent.
3. The general significance of *terminaisons en grappes* is discussed.
4. A description of the innervation of muscle spindles is given. The somatic motor innervation of the intrafusal fibres both in lower vertebrates and in mammals is confirmed.
5. Negative findings are reported with regard to the sympathetic innervation of striated muscle fibres and a criticism of Boeke's and Agduhr's original preparations is given.
6. The view is put forward that in striated muscle tissue sympathetic nerves supply only the blood vessels and are concerned only with the regulation of the circulation.
7. The possible mode of action of the sympathetic and of vaso-dilator nerves is also described.
8. The plurisegmental control of muscle fibres is discussed and new evidence is presented.

Appendix.

Remarks on the Innervation of the Gut and the Control of Peristalsis et cetera.

During the course of the investigation into the innervation of striated muscle other problems were considered and among these one of the most important was the innervation

of the gut. The main interest of this investigation was concerned with the relation and function of the sympathetic nerves. Observations on the striated muscle tissue were leading to the deductions set forth above in the main thesis and it was important to compare the findings there with those obtaining elsewhere. Pieces of the stomach and intestines were prepared according to the methylene blue and gold techniques and after being stained with methylene blue, besides spread preparations, pieces of tissue were blocked and sectioned in paraffin *et cetera.* Tissues were also prepared according to Kulchitsky's modification of Dustin's rapid Bielschowsky method, as described by Miss Hill.[60] The relations of the ganglia in the walls of the alimentary canal were also examined in sections fixed and stained according to the routine methods, namely, hæmatoxylin and eosin, Van Gieson and Mallory's triple staining method for connective tissue.

We were able to confirm generally many of the observations recorded by other investigators and have very little to add in this respect. It may be mentioned, however, that nerve cells were sometimes observed in the circular muscular coat. This was first demonstrated to the author by a colleague, Dr. Inglis, of the Pathology Department, University of Sydney, who found a nerve cell in the circular muscle coat in a section of an appendix. Although, then, the extensive series of observations made in this field have not been fruitful in bringing to light any new and particularly outstanding histological facts, yet one conclusion was arrived at which is of considerable importance in considering the question of the mechanism of intestinal movement. This was that the nerve fibres going to the plain muscle cells give rise to a great number of branches which end in relation to a large number of these cells, representing a very general type of innervation and not a specific one of individual cells. An individual cell may thus have a relation to the ends of more than one terminal branch or collateral branch of a nerve fibre (compare Hill and Tiegs[61]). This is not to be interpreted, however, as representing a double innervation of plain muscle cells as suggested by Tiegs.

With regard to the sympathetic nerves, it may be said that from our own observations and from those recorded in the literature it appears that there is no reason to suppose that they subserve a different purpose here than in striated muscle as described above, namely, that the sympathetic nerves are concerned with the maintenance of an efficient circulation.

One of the inherent properties of plain muscle tissues is that of automatic rhythmic contraction. This property and the existence between the muscle cells of intercellular connecting protoplasmic bridges, together with the findings of Carey[62] with regard to the helicoidal architectonics of the small intestines, provide a mechanism for the propagation of waves of contraction without the intervention of nervous tissue. Such a system, however, would tend to respond to every adequate mechanical stimulus and would lead to chaotic activity. The existence of the nervous plexuses provides a means of coordinating this activity and of providing a definite polarity, so that stimulation tends to cause peristaltic waves to pass in one direction. When a wave of contraction passes down the gut wall, the contractile cells pass through a refractory period after contracting, the length of such depending to a great extent on the mechanism which leads to recovery of its power to contract.

This mechanism is provided by the circulatory system which is under the influence of the sympathetic.

The plexuses which preside over the orderly activity of the muscle tissue, are again under the influence of a hierarchy of centres in the central nervous system and these coordinate its activity with that of the body as a whole. With regard to this, it is interesting to note that there seems to be a reciprocal control of the splanchnic and peripheral vessels, as witnessed by the existence of segmental tender areas in the skin associated with affections of the viscera. I have investigated this phenomenon and have often noticed that a tender or painful area can be very accurately mapped out and the viscus identified without the patient being consulted, because the areas are cold to the touch. This is in accord with the view put forward by Mills,[63] that pain is often associated with anoxæmia. This reciprocal control of the splanchnic and peripheral circulation may help to explain the beneficial effects produced by poultices and plasters *et cetera* which not only promote local circulation and relieve the pain, but probably reflexly promote more rapid circulation in the affected viscera. Langley,[64] in the account of his investigation on vascular reflexes, remarks that his results suggest that there are certain afferent fibres, proceeding from the viscera, which inhibit the part of the vaso-constrictor centre connected with the viscera and excite the part connected with the skin. Although we have a different conception of the way that these afferent fibres produce their effect, it is interesting to note that Langley's findings tend to support the idea of a relation between the innervation of the splanchnic and the peripheral vessels.

Returning to the mechanism of intestinal movement, we thus see that the inherent activity of the plain muscle tissue is regulated not only by a local reflex nervous mechanism, but is under the influence of the central nervous system through the extrinsic nerves, principally the vagus. It is significant that this external influence has greater control of the œsophagus, stomach and upper part of the small intestine than of the small intestines generally. This corresponds to the distribution of the vagus. Besides this direct control of the muscle cells there is the control of the blood vessels through the sympathetic nerves which indirectly influence the activity of the muscle cells. Stimulation of the local neurones, either locally or through the vagus, leads to increased amplitude and intensity of the peristaltic waves and increased circulation, brought about through the sympathetic, tends to lessen the refractory period, making possible increased frequency of contraction. Over-stimulation of the sympathetic (see thesis above) leads, as elsewhere, to vaso-constriction and here is associated with the phenomenon of inhibition.

This conclusion with regard to inhibition in the gut naturally leads to the consideration of the phenomena of inhibition in general. What, for example, is the mechanism of inhibition in the heart? If inhibition in the gut is due to alteration in the circulation, then, as the vagus has an inhibitory influence on the heart, we should have to postulate a vagal control of the circulation in the heart and the control of the heart muscle through the sympathetic. There is evidence that the heart muscle is under the direct influence of the sympathetic, but we had no evidence that the coronary circulation was under the influence of the vagus. This was a difficulty; but shortly after these conclusions were arrived at by theoretical deduction, Woollard[65] submitted evidence that led him to conclude that "ventricular muscle is supplied by sympathetic fibres only, and that although the larger branches of the coronary arteries were mainly innervated by the sympathetic, their smaller branches are supplied mainly by the vagus." Now, according to the view expressed in this paper it is just these smaller, more muscular walled arteries which have such an influence on the supply of blood to a part, so it appears that Woollard's findings tend to support the view of inhibition which is here put forward.

Conclusion.

Part of the foregoing thesis on nerve endings in striated muscle was submitted in application for the Peter Bancroft Prize in February, 1927, and the findings up to that date were summarized in Latham's article: "The Histological Evidence for the Sympathetic Innervation of Striated Muscle Fibres" ["Transactions of the Australasian Medical Congress (British Medical Association), Second Session," supplement to THE MEDICAL JOURNAL OF AUSTRALIA, November 26, 1927, page 433] which was read before the congress at Dunedin early in 1927.

In conclusion I wish to express my thanks to G. H. Bosch, Esquire, through whose generosity

mainly the investigation was enabled to proceed. I also wish to thank Professor Burkitt, of the Anatomy Department, whose private periodicals, reprints and text books were always gladly placed at my disposal, and Professor Stump, of the same department, for helpful criticism, suggestions and encouragement, and, finally, the members of the technical staff of the Anatomy Department for their ready and kindly assistance at all times and in all circumstances.

I wish also to take this opportunity of thanking my colleagues in Europe for their kindness and courtesy shown to me during my stay with them as a Fellow of the Rockefeller Foundation, especially Professors Boeke, Agduhr and Bielschowsky who so readily put their preparations at my disposal for the purpose of this investigation, and also Professor J. T. Wilson, Cambridge, and Professor G. Elliot Smith, London, for their valuable criticism during the final preparation of this manuscript.

EXPLANATIONS OF PLATES.

All figures, except those indicated, are photomicrographs. The objectives are Zeiss 8 millimetre ($\frac{1}{8}$ inch) apochromatic or Leitz 2 millimetre ($^{1}/_{12}$ inch) apochromatic. A "Makam" camera, Philips's "Point-o-lite" light source and a Conradi achromatic condenser were used.

FIGURE I.

Typical spray of ***terminaisons en plaque***; lizard. A *confluens capillorum* in relation to the ending (*a*) is well seen, but a similar arrangement of capillaries is seen in relation to the endings (*b*) and (*c*); 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE II.

Typical spray of *terminaisons en grappes*; lizard. Note the primitive sole-plate in relation to the ending (*a*). These endings arise from a leash of finely medullated fibres which come from the coarser medullated fibres in the lower left-hand corner of the figure. Note also the fine collapsed capillaries (*b*). Such capillaries are often accompanied by fine sympathetic nerve fibres, the endings of which sometimes appear to end in relation to the muscle fibres. Compare with Figures XXXIII and XXXIV; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE III.

A typical *terminaison en plaque* with its coarse fucoid or seaweed shaped fronds; lizard. Note the granular sole-plate with narrow clear area in immediate relation to the fronds and the larger clear areas which represent the nuclei of the sole-plate; 2 millimetre ($^{1}/_{12}$ inch) objective.

FIGURE IV.

A *terminaison en grappes*; lizard. This is ending (*a*) of Figure II. The fine nerves from which the ending arises are finely medullated and the sole-plate is clearly seen; 2 millimetre ($^{1}/_{12}$ inch) objective.

FIGURE V.

A typical large medullated nerve which ends in a typical *terminaison en plaque*; lizard, showing axone and myelin sheath. This sheath does not take up the stain, but a slight deposit of gold in the neurolemma indicates its extent. These fine lines which lie on either side of the axone and represent the neurolemma have been mistaken by some observers for fine nerve fibres which are sometimes described as accompanying the larger one. Creasing and folding of the neurolemma sometimes gives rise to artefacts, which have been mistaken for fine fibres twining around and accompanying the larger fibre; 2 millimetre ($^{1}/_{12}$ inch) objective.

FIGURE VI.

A finer medullated nerve going to a *terminaison en grappes*, lizard; 2 millimetre ($^{1}/_{12}$ inch) objective.

FIGURE VII.

Terminaison en grappes; lizard. This figure is submitted as evidence of the hypolemmal relation of the ending. Tension on the fibre has pulled the sarcolemma up into a cone. The fibre going to the ending is accompanied by a fine capillary with its sympathetic nerve. The capillary (Cap.) is seen leaving the figure to the left. Such endings as this show a marked disproportion between the individual fronds of the ending and the cross striations which are scarcely visible in the figure; 8 millimetre ($\frac{1}{8}$ inch) objective (see appendix).

FIGURE VIII.

Terminaison en plaque, lizard, showing medullated ultra-terminal collateral ending in a *terminaison en grappes* in relation to a smaller muscle fibre. Evidence of the motor nature of *terminaison en grappes*; drawing.

FIGURE IX.

Terminaison en plaque, lizard, with medullated terminal collateral ending on an intrafusal fibre of a muscle-spindle. Evidence of the motor nature of *terminaison en grappes* and also of the motor innervation of an intrafusal fibre. Part of the sensory ending of the spindle is shown to the left of the figure. The complete sensory ending is about ten times as long as the fragment shown; drawing of the relations of the nerves only.

FIGURE X.

Terminaison en plaque, lizard, with a finely medullated collateral giving rise to three grape-like terminations on two smaller muscle fibres; drawing.

FIGURE XI.

Two terminal collaterals of a motor fibre, lizard, one of which ends in an almost complete *terminaison en plaque*, while the other ends in a *terminaison en grappes*; drawing.

FIGURE XII.

Early form of *terminaison en grappes* (M) on end of a non-medullated fibre and lying in relation to a 16 μ muscle fibre; lizard; 8 millimetre ($\frac{1}{8}$ inch) objective. Retouched.

FIGURE XIII.

Three developmental forms of motor endings, lizard: (*a*) *Terminaison en grappes* lying in relation to a 16 μ fibre; (*b*) a larger *terminaison en grappes* whose fibre is finely medullated almost up to ending (*c*) which is a large *terminaison en grappes* on a larger muscle fibre and is supplied also by an incompletely medullated fibre; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE XIV.

Four forms of motor endings: lizard, (*a*) *Terminaison en grappes* supplied by two fine non-medullated fibres; (*b*) *terminaison en grappes* on a larger muscle fibre and supplied by an incompletely medullated fibre, tension in which is seen pulling up the sarcolemma; (*c*) a large *terminaison en grappes* of a medullated fibre; (*d*) a typical *terminaison en plaque* in profile and slightly out of focus. This figure is composed of two photographs of the same field but taken at slightly different focuses; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE XV.

Two *terminaison en grappes*, lizard, of which (*b*) represents almost the final stage, in which the nerve is medullated almost up to the ending. The individual fronds have not yet developed into the coarse fucoid or seaweed shaped fronds of a typical fully developed motor ending as shown in Figure III; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE XVI.

Another almost fully developed *terminaison en plaque*. The motor plates of the python described in the text are similar to this; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE XVII.

Terminaison en plaque, lizard, with ultra-terminal collateral ending on the same muscle fibre as the plate from which it arises; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE XVIII.

Terminaison en plaque, lizard, supplied by two coarsely medullated terminal collaterals of a motor nerve; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE XIX.

Terminaison en grappes, lizard, arising as an ultra-terminal collateral from another *terminaison en grappes* and ending in another muscle fibre; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE XX.

Terminaison en grappes; frog. The fibre is finely medullated and can be traced back until it is seen to come off a coarser medullated nerve which ends in typical motor plates; 2 millimetre ($^{1}/_{12}$ inch) objective.

FIGURE XXI.

Typical spray of the finer filiform types of motor endings seen in the frog's muscle; 8 millimetre ($\frac{1}{8}$ inch) objective.

FIGURE XXII.

A typical fully formed motor ending in a frog. The motor endings in the frog are elongated in the direction of the long axis of the fibre (compare with Figure XXI) and has coarse fucoid fronds similar to those found in the lizard; 2 millimetre ($^1/_{12}$ inch) objective.

FIGURE XXIII.

Ultra-terminal collateral of a motor ending, frog, terminating on another muscle fibre which is already supplied by a motor ending; drawing.

FIGURE XXIV

A typical motor ending; tuatara lizard. These plates resemble those found in birds; 8 millimetre (⅙ inch) objective.

FIGURE XXV.

Another motor ending from a tuatara lizard, showing a stage in development earlier than those shown in Figure XXIV. It is supplied by two medullated nerves; 8 millimetre (⅙ inch) objective.

FIGURE XXVI.

Motor *terminaison en grappes*; tuatara lizard; 8 millimetre (⅙ inch) objective.

FIGURES XXVII and XXVIII.

Muscle spindle from *Musculus panniculus carnosus* of the echidna, showing the complete sensory (Figure XXVII) and the complete motor (Figure XXVIII) innervation. The motor endings (*b*) in Figure XXVIII are on fibres which arise as collaterals of motor nerves which end on extrafusal fibres, as shown at (*a*); 8 millimetre (⅙ inch) objective.

FIGURE XXIX.

Further evidence of the motor innervation of an intra-fusal fibre of a muscle spindle in lizard. This example is similar to that shown in Figure IX; 5 millimetre (⅛ inch) objective.

FIGURE XXX.

Motor endings in extrinsic eye muscle of a rabbit. Fragments of the fine branches of the plexus of sensory nerves are seen ending in relation to the muscle fibres; 8 millimetre (⅙ inch) objective.

FIGURE XXXI.

Another figure showing some of the fine sensory fibres in the extrinsic eye muscles of the rabbit. These figures give only a suggestion of the enormous number of sensory terminations in these muscles; 8 millimetre (⅙ inch) objective.

FIGURE XXXII.

Drawing of a more finely teased preparation of a piece of extrinsic eye muscle of a rabbit, showing sensory nerves which can be traced back until they are seen to arise from the extensive plexus of medullated sensory nerves.

FIGURE XXXIII.

Muscle spindle, frog, showing the connexion between the sympathetic fibre on a blood vessel (B.V.) and the sympathetic nerves of blood vessel in the spindle. The blood vessel of the spindle is faintly stained and can be seen between the sympathetic fibre near the point of the arrow and the dense mass of spindle endings; 8 millimetre (⅙ inch) objective. Retouched.

FIGURE XXXIV.

Typical motor endings of a bandicoot, showing sympathetic nerves (Sym.) which accompany blood vessels. Although the blood vessels are distinctly visible under the microscope, they are slightly out of focus and are only faintly stained. The fibre ascending to the top of the field could easily be mistaken for a sympathetic nerve going to a sole-plate, but examination of the specimen reveals its relation to a capillary and it passes out of the field without giving off any ending to the sole plate; 5 millimetre (⅛ inch) objective.

FIGURES XXXV and XXXVI.

Typical blood vessels with muscular walls and accompanying sympathetic nerves. The sympathetic nerve can be traced through many fields along the various capillary branches of the blood vessels, but no endings are found to pass off to end in relation to the muscle fibres; 8 millimetre (⅙ inch) objective.

FIGURE XXXVII.

Terminaison en plaque, lizard, in profile on a muscle fibre showing the cross-striations, which are not always continuous, but in places appear broken. The tips of some of the fronds in the plate and the clear area immediately in relation to the fronds are seen. Careful observation of many such specimens under the most critical conditions failed to reveal any neurofibrillar connexion between the ramification of the axon and the cross-striation. Note also the disproportion between the size of the fronds and the cross-striations. This photograph does not show the clear oval areas often seen in such specimens, which represent the nuclei of the sole-plate; 2 millimetre ($^1/_{12}$ inch) objective.

FIGURE XXXVIII.

Drawing showing typical mode of termination of a motor fibre; cat. Occurs in more than 90% of fibres in *musculus interosseus.* V is a small varicosity on the non-medullated part of the axone.

FIGURE XXXIX.

Drawing showing variation from the normal mode of termination of the motor nerves. Occurs in less than 10% of fibres in the same muscle as in Figure XXXVIII.

FIGURE XL.

Drawing showing artefacts in the neurolemma sheath which sometimes simulate fine fibrils.

FIGURE XLIA.

Drawing (H.J.W.) of Boeke's preparation which he figures in his article (Boeke,[5] Figure XV). See text.

FIGURE XLIB.

Boeke's original figure reproduced for comparison.

FIGURE XLII.

Drawing (H.J.W.) of one of Boeke's "sympathetic" endings in eye muscle. See text.

FIGURE XLIIIA.

Drawing (H.J.W.) of Boeke's preparation which he figures in his article (Boeke,[5] Figure XIII). See text.

FIGURE XLIIIB.

Boeke's original figure reproduced for comparison.

FIGURE XLIVA.

Drawing (H.J.W.) of Boeke's preparation which he figures in his article (Boeke,[5] Figure VI). See text.

FIGURE XLIVB.

Boeke's original figure reproduced for comparison.

FIGURE XLV.

Drawing (H.J.W.) of one of Boeke and Barenne's "sympathetic" endings in *musculi intercostales.* See text.

FIGURE XLVI.

Drawings (H.J.W.) of some endings seen in Agduhr's slides. "d" is very faintly stained and was found in a preparation from six days' degeneration material. The others are from five days' degeneration material. See text.

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Reports of Cases.

"MIGRAINE OPHTHALMOPLÉGIQUE" (CHARCOT).[1]

By Eric Susman, M.B., Ch.M. (Sydney), M.R.C.P. (London),

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W.E., male, *ætatis* thirty, complained of regularly recurring attacks of left-sided headache, accompanied by

[1] The patient described herein was shown at a meeting of the New South Wales Branch of the British Medical Association on August 8, 1929.

nausea and vomiting, since the age of two. The attacks always ran true to type. They occurred once a fortnight, lasted from twenty-four to forty-eight hours and went away only after a good night's rest. They started early in the morning. There was always a definite aura, to wit, a nervous, jumpy, restless, excitable condition on the evening preceding the inauguration of an attack, a feeling, as he expressed it, as if something very serious was going to happen.

At the age of fourteen, after a particularly severe bout, the patient noticed that his left eyelid drooped. It would remain down for two days following the attack and then go back to its normal position. From the age of fourteen until six months ago this temporary ptosis had occurred in every attack. Since then the eyelid had remained down even during the intervals.

At the age of seventeen his left eye would swing outwards during each attack and after one year remained out permanently. He had been continually distressed by troublesome diplopia which was only relieved a few months ago, when the ptosis became permanent.

On examination the only abnormal physical signs were left ptosis, a left external strabismus and a large fixed dilated left pupil. In other words there was a complete infranuclear left oculo-motor paralysis. The corneal reflexes were present and equal, the optic discs were healthy and the blood serum failed to react to the Wassermann test. Like that of most migrainous subjects, the patient's intellectual standard is high. Although, as a direct result of his malady he lost much schooling, he succeeded in winning many prizes.

Comment.

This, then, is the case of a man, a life-long sufferer from typical migraine, who after many years developes a temporary paresis of a part of his oculo-motor mechanism. After a variable period this temporary paresis becomes a complete and irrecoverable permanent paralysis. Such is that rare but highly important condition of ophthalmoplegic migraine. In this syndrome the paralysis always occurs on the side of the headache. The third nerve is more frequently affected than the sixth, according to Foster Moore.[1] On the other hand, Collier[2] maintains that the sixth nerve is more commonly involved. Occasionally both suffer. When the third nerve is affected, the external fibres suffer more severely, the fibres subserving pupillary function apparently being more resistant.

It is difficult to postulate an organic pathological change for migraine. And it is from the pathological aspect that these rare cases of ophthalmoplegic migraine (and the same applies to migraine with temporary, going on to permanent hemianopia) are so important. For it is certain that there must be some gross intracranial lesion to produce such serious results. A speculative pathological change is a vasomotor disturbance which has "just gone a bit too far," the arterial spasm having produced a sufficient degree of ischæmia to injure the parts permanently and irreparably. Spitzner whose *post mortem* specimens are at Baltimore, has demonstrated unilateral hydrocephalus on the side corresponding to the headache. He suggested that this condition was due to a temporary swelling of the chorioid plexus, thus plugging the foramen of Munro. If this be true, one can then easily imagine that frequent and repeated squashing of the oculo-motor nerves in their intracranial course from the downward pressure of a much dilated lateral ventricle would ultimately bring about a cessation of neuronic function. The further study of this interesting malady will probably be the means whereby migraine in general will be lifted from the dustbin of functional diseases and transported to the more pleasant and purer atmosphere of organic neurology. And so, for the present, we must leave it at that.

References.

[1] R. Foster Moore: "Medical Ophthalmology," Second Edition, page 159.

[2] James Collier: Price's "Textbook of Medicine," page 1443.

Reviews.

TROPICAL DISEASES.

THOSE familiar with previous editions of Stitt's well known hand book on the diagnosis and treatment of tropical disease will scarcely recognize its fifth edition.[1] Besides extensive revision several new sections have been added, the most important of these being on tropical hygiene. So much enlargement has taken place that this book should no longer be regarded as a hand book; it should be included among the text books on tropical medicine. A considerable amount of overlapping has taken place between this work and a companion work by the same author, namely "Practical Bacteriology, Blood-work and Animal Parasitology." We wonder whether it would not have been advisable for the author to have considered combining both volumes in a complete work embracing tropical medicine, tropical laboratory work and tropical hygiene in three volumes of smaller size. We realize the convenience to the tropical worker in having all the information in one volume, but when a volume ceases to be of hand book size, then this advantage of unity disappears.

It is interesting to note that yellow fever is classed as being due to a filterable virus, a belief long held by the British School. Stitt also mentions the work in Nigeria which proved that several close relatives of *Aedes argentus* are efficient vectors of yellow fever.

The theory advanced by Stitt that yaws and syphilis are one and the same disease will be repugnant to most British tropical practitioners. He bases this hypothesis on the fact that yaws is so purely tropical that it probably demonstrates climatic influence on syphilis. He also advances as supporting evidence the fact that in Hayti arterial degenerations are found in natives with histories of yaws. Surely both these facts are capable of explanation. All authorities recognize the very close similarity of the causative organisms of the two diseases and most have presupposed a certain immunity conferred by one against the other. It is unreasonable to suppose the earlier and more superficial lesions of syphilis might not be prevented by an earlier attack of yaws. Again, if yaws is a climatic manifestation of syphilis, why do not white colonists in the tropics manifest yaws rather than syphilis?

It would have seemed better to have made the connexion between amœbic dysentery and liver abscesses a little plainer rather than to have treated them as separate diseases. In malaria no mention is made of the very real danger of tetanus following intramuscular injections of quinine solutions.

A few minor errors in the text and in the distribution of disease were noted, no doubt due to the complete alteration in the setting up of the work.

The section on animal parasites, arthropods, fish, snakes *et cetera* has been revised. The section on snakes has obviously been written for the American reader and the Australian will be well advised to follow the recent valuable work of Fairley, Kellaway and their fellow workers. The ordinary reader will lament that euphony has been sacrificed to nomenclature when he observes that the name *Filaria bancrofti* has been changed to *Wuchereria bancrofti*. Does this mean that we shall now have to include the disease "wuchereriasis" in our diagnoses?

Despite the above criticisms which are, after all, of a minor nature, the work ranks as one of the first four works on tropical diseases published in the English language. The printing is clear and the binding stout and attractive. The work can confidently be recommended not only to the student, but also to the practitioner as a sound and up to date presentation of the subjects with which it deals.

[1] "The Diagnostics and Treatment of Tropical Diseases: A Compendium of Tropical and Other Exotic Diseases," by E. R. Stitt, A.B., Ph.G., M.D., Sc.D., LL.D.; Fifth Edition, Revised. Philadelphia: P. Blakiston's Son and Company. Royal 8vo., pp. 933, with illustrations. Price: $9.00 net.

The Medical Journal of Australia

SATURDAY, NOVEMBER 30, 1929.

Coordinated Research.

EVERY practising member of the medical profession encounters in his daily work problems that admit of no immediate solution. Notwithstanding all the investigations, observations and discussions, the complete story of the ætiology, pathogenesis and pathology of even common diseases has not yet been told and the practitioner who is called upon to attend persons suffering from various diseases, realizes that he is rarely able to conquer the pathological process and repair the damage already done. The literature on each disease or group of diseases has attained such immense proportions that it has become unwieldy. Apart from the facts that very many journals and other publications are inaccessible and that few medical practitioners can read and understand more than two or three languages, no one with a busy practice could find time to read a tithe of what has been written on the common diseases. The complexity of the problems, their intrinsic difficulty and the lack of uniformity in the point of view have led to the multiplication of specialties and the gradual establishment of water-tight compartments in research. The practitioner finds himself more and more bewildered as each specialist attacks the problems of causation from his own point of view. There has been a tendency in recent years to form teams in hospitals and research institutes for the purpose of attacking the problems of disease from several points of view simultaneously, but even under these conditions it is by no means common for the results of investigation and of observation to be coordinated by an impartial judge.

The proposal was put forward some years ago by the members of the Royal Commission on Health that a medical research council should be created by the Department of Health of the Commonwealth. More recently the Federal Committee of the British Medical Association in Australia has urged the Federal Government to give effect to the recommendation of the Royal Commission in connexion with the establishment of a medical research council and added to this request a suggestion that the workers should be independent of the Public Service Regulations and that the personnel of the council should consist essentially of research workers and representatives of Parliament. It appears that the Federal Committee has in mind the constitution of the Medical Research Council of the Privy Council. The formation of this body has been discussed on several occasions in these columns. It arose as the Medical Research Committee appointed under the provisions of the *National Insurance Act*. In 1919 the Committee was changed into a council of the Privy Council, as it was found that the conditions of research in Great Britain demanded more autonomy and greater elasticity than could be given it under the act. The personnel of the Medical Research Council leaves little to be desired. The chairman is the Earl of Balfour, whose erudition, scientific and philosophical education and critical ability are recognized throughout England, Scotland and Ireland. Lord Mildmay of Flete is the treasurer and the Right Honourable Sir Charles Trevelyan is the third Parliamentary representative. The eight professional members are eminent investigators, teachers and authorities in one or other branch of medical science. Each one is a Fellow of the Royal Society as is the secretary who is also a scientist of renown. The Medical Research Council works largely through special committees, the members of which are selected with care and due consideration of the nature of the problems to be investigated and the past achievements of the chosen workers. Much of the work undertaken for the Medical Research Council, however, is individual work. A single investigator conducts the research and presents his or her report. Apart from the short preface inserted by the Council, there is no comment on the significance, reliability or acceptability of the findings, nor is any attempt made to coordinate the work of several specialists on one

subject. The Medical Research Council has been responsible for a great volume of published matter. Much of it is excellent and some of it is authoritative. On the other hand the Council claims a great deal of research which it has not initiated or directed, although it has made some monetary contribution towards the associated expenses.

In Australia the number of research workers is still somewhat limited. With the exception of the Walter and Eliza Hall Institute and the Baker Institute the research work conducted up to the present has been conceived and accomplished by one or two individuals. Recently the Cancer Research Committee has introduced a campaign of coordinated effort aiming at the elucidation of the biology, physics, chemistry and physical chemistry of X radiation. The idea of coordination has become firmly established in the minds of many of the research workers, but there are still many difficulties to be overcome before these ideas can be translated into practice save on a small scale. If a medical research committee or council is to be established in Australia and all are agreed that there is an urgent need for it, its chief function should be to stimulate investigations from many points of view into chosen problems and to coordinate the findings of the workers, so that every avenue of approach may be explored and the evidence adduced by each specialist may be properly evaluated. It would be advantageous if the committee or council could be independent of official control, if it could be privately endowed and morally rather than legally responsible to the public. Its constitution should be determined by the medical profession and its members elected by that body with assistance from men of high commercial standing. Under the existing conditions there would be no necessity to create or establish institutions. If the committee or council gained the confidence of the research workers, it could take such steps as might be necessary to converge the efforts of individual investigators towards one or a few objectives and it could coordinate those efforts and act as a clearing house for the findings. Care would be taken not to destroy individuality or originality, while each worker would still be at liberty to develope his own ideas and to follow out any line of reasoning that might appear to him to be worth following. The committee or council would prevent waste by unnecessary repetition of work already completed and would be the means of adjusting the endeavours of men working in different parts of the Commonwealth.

Current Comment.

GASTRIC AND DUODENAL ULCER.

The diagnosis of gastric and duodenal ulcer is usually straightforward and simple. The history given by the patient and the results of examination, clinical, laboratory and radiological, leave little doubt as to the nature of the pathological process. When the patient is submitted to surgical operation, an opportunity occurs for verifying the preoperative diagnosis. If medical treatment is adopted, verification must be made by the clinical improvement and by the change in response to laboratory tests and radiological examination. Sometimes autopsy alone gives the opportunity. Gastric or duodenal ulcer may not, however, be the only condition present. The associated lesion may or may not produce an alteration in the clinical picture. In either case a mistake in diagnosis may result. H. R. Hartman and A. B. Rivers have recently reported from the Mayo Clinic the results of the study of 1,075 patients in whom ulcerating lesions of the stomach or duodenum were found at operation.[1]

They sought to determine what conditions might remain masked in the ulcer syndrome and to discover whether more careful diagnosis would be of benefit to the patient. The only patients included in the series were those in whose histories a diagnosis of a single lesion, gastric or duodenal ulcer, was made before operation. When tissue was removed, the pathologist's diagnosis was accepted as final, but when no tissue was removed, the surgeon's diagnosis was accepted. The patients with duodenal ulcer numbered 700 and those with gastric ulcer 375. Unfortunately no figures are given in regard to the total number of patients in whom a diagnosis of gastric or duodenal ulcer was made. At first sight it would appear that operation was carried out much more frequently in duodenal ulcer than in gastric ulcer. This would be surprising, for while total excision of gastric ulcer is often undertaken, the same cannot be said of duodenal ulcer and the value of gastro-enterostomy in duodenal ulcer has been doubted by many. It may be that more patients are seen at the Mayo Clinic with duodenal ulcer than with gastric ulcer. In a matter of this kind not only has the question of cause, predisposing or actual, and effect to be considered, but that of the element of chance in the simultaneous

[1] *Archives of Internal Medicine*, September, 1929.

occurrence of the two conditions. This point is, however, really incidental to the present inquiry. Among the 700 patients with duodenal ulcer 38% had duodenal ulcer as the sole abnormality found at operation. In 62% some pathological entity, not specified before operation, was found to be associated with the ulcer. A diagnosis of diseased appendix was made by the operating surgeon in 51·8% of all the patients of the series; in only 7·4% was the appendix acutely or subacutely inflamed. The conclusion is that 14·3% of all cases of appendicitis in patients operated on for duodenal ulcer appeared to be of noteworthy significance. The question of chronic appendicitis will be referred to later. In 3·6% of the 700 patients distinct cholecystitis was found and in the same percentage there was an associated gastric ulcer. There were eight patients among the 700 in whom gastric ulcer only was found after the clinician, basing his opinion mainly on the radiological findings, had made a diagnosis of duodenal ulcer. Among a miscellaneous group of 3% were such conditions as duodenitis without actual ulcer, benign tumours, Meckel's diverticulum, duodenal diverticulum, carcinoma of the stomach.

Among the 375 patients in whom a diagnosis of gastric ulcer was made, this lesion only was found in 50·8%. Associated appendicitis was reported by the surgeon in 38·8% of the group, but in only 3·1% of these was the appendix affected by either acute or subacute inflammation. Duodenal ulcer was found in association with gastric ulcer twenty times or in 5·2%. Cholecystitis was found eight times, 2·1%. In 2·1% of the group changes were found which gave rise to a suspicion of the presence of malignant disease. Reference will be made to this later. Among the more unusual lesions found in these patients were Lane's kink, calcareous lymphatic glands of the jejunum, splenitis and gastritis without pathological evidence of gastric ulcer.

The first point to be considered in regard to these findings is the association of appendicitis with peptic ulcer. The authors state that the association observed with chronic appendicitis should not be considered of great importance, because it is extremely doubtful whether the presence of this complication was in any way contributory to the symptoms for which the patient sought relief. At the same time, they regard acute or subacute appendicitis as of definite importance. The signs and symptoms of acute appendicitis are generally definite and distinctive, but at the same time they may present difficulty. In spite of this the conclusion of Hartman and Rivers will be generally conceded, that acute appendicitis will as a rule present features which are sufficiently definite to regard to chronic appendicitis, if by that term is be indicative of its presence. Their statement in meant the sequelæ of a definitely acute attack, may not gain general acceptance, especially in view of the work of Braithwaite in regard to the lymph flow from the ileo-caecal angle which was discussed in our issue of December 1, 1923, and the further findings of Berceanu in regard to the reception of appendiceal lymph by duodeno-pancreatic glands which was discussed in the issue of August 23, 1924. It must be presumed that in every instance sections were made of the appendiceal wall and that these were submitted for microscopical examination.

The next point for consideration is that of the association of malignant disease. The figures quoted by the authors show that appearances suggestive of malignant disease are much more likely to be found when a diagnosis of gastric ulcer is made than when duodenal ulcer is suspected. In only one instance of the 700 in the latter group was malignant disease found and in this instance it was situated on the proximal side of the pylorus. Attention is drawn by Hartman and Rivers to the fact that in no instance was any suggestion made before operation that malignant disease might be present. Of greater significance is the fact that the surgeon was frequently wrong in his supposition, because many of the patients are living and apparently in good health in spite of the fact that the lesions were not removed at the time of the operation. Short accounts are given of the histories of eleven patients in whom supposedly malignant growths were found. In many instances no details of the operation are stated and the ulcer was not removed. It is pointed out that the surgeons did not record the criteria adopted by them in arriving at their decisions. The conclusion in regard to the examination of portions of an ulcer before it is declared to be malignant, is obvious. Occasionally the thickening around an ulcer may be so hard as apparently to justify a diagnosis of malignant disease, but after the performance of gastrojejunostomy or the draining of an affected gall bladder the infiltration may in large measure disappear.

It is interesting to note that cholecystitis was found in 3·6% of the patients regarded as suffering from duodenal ulcer and in 2·1% of those regarded as suffering from gastric ulcer. Until the causation of peptic ulcer is definitely known, it is impossible to determine any relationship between these two conditions. If cholecystitis is not acute, it will be very difficult to diagnose its presence in association with a peptic ulcer which is producing typical symptoms.

The general conclusion of Hartman and Rivers is that when at least the more frequent lesions associated with peptic ulcer are borne in mind, the probability of accurate diagnosis will be increased. It must be remembered that even with the greatest care some of the lesions associated with peptic ulcer will not be discovered. The chief thing is that the possibility of their presence should be kept in mind. This is most necessary as far as malignant disease is concerned. The removal of such a complication as cholecystitis or appendicitis will often hasten recovery from the ulcer.

Abstracts from Current Medical Literature.

DERMATOLOGY.

Sclerema Neonatorum.

J. SKEER (*Archives of Dermatology and Syphilology*, May, 1929) reports a patient with *sclerema neonatorum* treated and cured by X rays. The patient, aged two months, was given three doses of X rays over the back, buttocks, thighs and calves. The doses were one-third of a skin erythema unit and were given at intervals of approximately three weeks. By three months the thickening had definitely decreased and at the end of six months the child was apparently cured. The child began to walk at thirteen months.

Phytopharmacological Examination of the Blood.

I. R. PELS AND D. I. MACHT (*Archives of Dermatology and Syphilology*, April, 1929) describe a phytopharmacological method developed by one of the authors of examining the blood serum for toxicity. A series of patients with dermatoses was tested and the results are tabulated. These tests were made by noting the effect of the serum in the growth of young seedlings of *Lupinus albus* in the same manner as studies of the serum obtained from patients with pernicious anæmia have recently been carried out. It was found that the serum from a number of patients with pemphigus gave consistently abnormal and low readings, thus indicating a greater toxicity of such serum for plant protoplasm. Details and comments on the method employed are given and references are made to the more recent literature bearing on the theory of a toxicosis in the ætiology of pemphigus.

Syphilis.

J. A. KOLMER AND A. M. RULE (*Archives of Dermatology and Syphilology*, July, 1929) discuss the spirochæticidal activity of human syphilitic serum and the immunological significance of the Wassermann reaction. After a considerable amount of experimental work on rabbits, details of which are described by them, they have made certain observations which are essentially in agreement with similar work by Finger and Landsteiner on monkeys. They have found that freshly prepared serum from patients suffering from chronic, latent and active syphilis which yielded a positive response to the Wassermann test, was no more spirochæticidal *in vitro* than the serum of non-syphilitic patients. Four intravenous injections of serum from patients with chronic syphilis who yielded reactions to the Wassermann test, were given every day to rabbits suffering from testicular syphilis. The doses which varied from two to three cubic centimetres per kilogram of weight, had no more appreciable effects on the lesion than injections of similar amounts of serum from healthy non-syphilitic persons. It was also noted that intravenous injections of serum from syphilitic and non-syphilitic persons were without prophylactic activity when injected into rabbits which had received intratesticular inoculations with *Spirochæta pallida*. Apparently no part of acquired immunity in syphilis is essentially humoral because of the absence of demonstrable spirochæticidal antibody in the serum. The Wassermann antibody is neither spirochæticidal nor associated with spirochæticidal substances in syphilitic serum. Its presence may, however, be an index of tissue immunity in this disease. Serum prophylaxis and treatment of syphilis are not possible by present methods.

The Chloride Content of Whole Blood in Eczema.

N. BURGESS (*Archives of Dermatology and Syphilology*, July, 1929) gives the results of an investigation into the possibility of a disturbed chloride metabolism in eczema. The estimation of the chloride content was made according to the method of Whitehorn. As a preliminary check a number of normal persons was tested. The figures obtained are tabulated and the author points out that they correspond closely to those previously given by Myers. The author investigated the chloride metabolism of patients suffering from acne, pruritus and pemphigus, as well as of those suffering from acute and chronic eczema. The results obtained reveal no abnormality of chloride metabolism in any of those examined. There is therefore no indication for attempting to reduce the chloride content of the tissues by giving a salt-free diet or aiding the elimination of chlorides from the body. Any satisfactory results obtained by the intravenous administration of sodium thiosulphate to patients with eczema would appear to depend on some factor other than the alteration of the chloride content of the blood.

Leucoderma.

H. C. L. LINDSAY (*Archives of Dermatology and Syphilology*, July, 1929) states that in a percentage of patients with leucoderma the condition is secondary to fungus infections, syphilis, leprosy and many scaly eruptions such as psoriasis. He also attributes some instances of leucoderma to the action of the sun's rays, altered photosensitivity playing an important part. The author has found that gold sodium thiosulphate acts satisfactorily in counteracting excessive photosensitivity. He reports three cases. A boy of sixteen years was so improved that no abnormality could be detected in a photograph. The doses were given at intervals of a week, the first dose being 30 milligrammes and the others 100 milligrammes. A woman, thirty-four years of age, who had pronounced lesions on the left arm, received at intervals of a week three doses of 0·05, 0·1 and 0·1 gramme. Her injections were continued later on. At the time of publication this patient's improvement was not so pronounced. The third patient reported by the author was a medical student whose condition was almost cured when the author wrote.

Amycotic Dermatoses Simulating Mycotic Infections.

J. H. MITCHELL (*Archives of Dermatology and Syphilology*, April, 1929) claims that there are many dermatoses of the hands and feet which resemble mycotic infections and which are probably due to other causes. It is suggested that many of them are due to coccal infections and that there is frequently a concomitant paronychia which may act as a primary cause. He does not agree that because fungus occurs on the feet, therefore the lesion on the hand, when no fungus can be found by smear or culture, has a similar ætiology. There is also the question of a trichophyton to be considered. Many such conditions he finds are easily cured with solutions of potassium permanganate.

UROLOGY.

Treatment of Teratoid Tumours of the Testis.

A. L. DEAN, Junior (*Journal of Urology*, January, 1929) states that when a patient is found to have a malignant tumour of the testis and no metastatic lesions can be discovered, the treatment of choice consists in a thorough irradiation of the testis and of the abdomen on the same site followed in four to six weeks by orchidectomy. Several courses of irradiation should follow the operation at intervals as short as the toleration of the patient will allow. The operative removal of metastases from such tumours should not be attempted. Maximal irradiation by means of the radium pack and high voltage X rays offers a far greater chance of permanent relief.

Pyridium as a Urinary Tract Antiseptic.

H. W. E. WALTHER (*Zeitschrift für Urologie*, October, 1929) states that pyridium possesses the following particular characteristics: It has a particular power of stimulating epithelial cell proliferation, it has powerful bactericidal properties, it is capable of protecting the tissues and is rapidly excreted through the urogenital tract. The average dose is 0·2 gramme by mouth three times a day. Care must be taken not to drink too much fluid. The concentration of the drug in the urine will in these circumstances easily reach one in 2,000 which is an effective bactericidal concentration. During the excretion of the drug the colour of the urine varies from orange-yellow to garnet, while the stools are scarcely or not at all coloured. One important finding is that vesicular and prostatic massage during the exhibition of the drug

shows that these secretions have been regularly coloured yellow. In eighteen years' urological practice the author has not encountered a drug with such a prompt and energetic action in bacteriuria. from the first dose a retardation in the growth of bacilli and cocci, and especially gonococci, is noticed.

Suture of the Renal Pelvis and Ureter After Incision.

A. E. GOLDSTEIN (*Journal of Urology*, July, 1929) has compared the post-operative histories in patients submitted to suture and those not submitted to suture of the pelvis and ureter after operative incision of these cavities. The conclusion reached is that the non-suture operation is superior by far when the incidence of the post-operative complications is taken into account. Leaving the urinary tract incision open allows blood clot or urine to escape freely if anything is blocking its path along the ureter and as an indirect result of such freedom of escape post-operative infective complications are lessened.

Pneumo-Pyelography.

T. GOLDENBERG (*Zeitschrift für Urologie*, 1929, Special Number, *Deutsche Gesellschaft für Urologie*) declares that pneumo-pyelography deserves a much more frequent application in the elucidation of surgical urological problems. Even in stout patients the fine details given with air pyelograms are almost as good as with fluid media. The most important indication for pneumo-pyelography is when a urinary calculus is suspected, but is not visible in the plain radiogram. In these circumstances also pneumo-pyelography is of inestimable value in localization of the calculus, for it shows exactly in which part of the hollow interior of the kidney the offender lies. It is very easily carried out and if properly performed is quite without danger. There are no irritating after-effects on the patient, as there so often are with fluid media. If it is deemed necessary to add it to the examination, chemo-pyelography can be carried out as usual as soon as the air has been allowed to escape from the catheter, but it must be remembered that chemo-pyelography must never precede pneumo-pyelography or fallacies in interpretation will arise. Where there has been recent renal bleeding or where there is a suspicion of renal tumour, pneumo-pyelography is definitely contraindicated.

Pseudo-Membranous Trigonitis.

E. CANNY RYALL (*British Journal of Urology*, September, 1929) describes a condition appearing to the cystoscopist as a more or less transparent veil of a greyish-pink colour, completely or partially covering the trigone of the bladder and sometimes extending into the urethra. The author calls this pseudo-membranous trigonitis and states that it is peculiar to the female bladder. The symptoms are frequency which may be accompanied by urgency, present both day and night, pain usually at the end of the act, tenesmus which may be severe. The urine is either sterile or only slightly infected. Hæmorrhage is very rare. Medicinally sandalwood oil in 0·6 mil (ten minim) doses or better still creosote in 0·3 mil (five minim) doses is useful together with local instillations of silver nitrate varying in strength from 1% to 6%.

Routes of Absorption in Hydronephrosis.

D. M. MORISON (*British Journal of Urology*, March, 1929) has introduced dyes into the renal pelvis in hydronephritic kidneys of laboratory animals in amounts that were well below the pelvic capacity. By this means all traumatic entry into the veins, tubules *et cetera* was avoided with certainty. The experiments lead to the conclusion that the so-called "pyelovenous backflow," described by Hinman and Lee-Brown, is probably due to trauma and cannot be regarded as a usual factor in the mechanism of hydronephrosis. Two routes of absorption were noted, lymphatic and tubular. At the outset of complete ureteric obstruction there ensues for the first two or three days a purely lymphatic absorption from the walls of the renal pelvis and ureter. After about the third day tubular absorption commences and continues more actively than the lymphatic.

Extravesical Ureteric Openings in Women.

S. PERLMANN (*Zeitschrift für Urologie*, February, 1929) states that in women who can empty the bladder in a normal manner and yet suffer from a continual dripping away of the urine, it is necessary to think of the possibility of an extravesically placed ureteric orifice. Exact diagnosis is made possible by cystoscopy and pyelography. When the pyelographic appearance of a "double" kidney with two completely separate ureters is obtained, the efficiency of the lower half of this kidney should first of all be determined, for this is always connected with the normal ureteric orifice. The abnormal orifice which opens lower down (in the urethra, vagina or elsewhere) is connected with the upper half of the kidney. If the efficiency of the lower half of the kidney is good, then the upper half together with the corresponding ureteric tube, should be resected. In order to prevent bleeding from the wound in the kidney, a free muscle graft should be attached to the site of this wound.

Studies in Intravenous Pyelography.

A. ROSENO (*Zeitschrift für Urologie*, 1929, Special Number, *Deutsche Gesellschaft für Urologie*) publishes a preliminary report on his researches in the problem of securing satisfactory pyelograms and ureterograms after intravenous injections of radio-opaque substances. The object of developing this method is to render the whole procedure much more convenient both for the patient and the surgeon than it is at present by the usual cystoscopic method. The primary difficulty is that the renal pelvis and the ureters are not "storing organs" like the gall bladder and substances excreted into them are passed through quickly and are never in sufficient concentration to cast shadows on the X ray film. By experiments it has been discovered that when the bladder is very full, the rate of flow of urine down the ureter is retarded. The author therefore advises arranging the intravenous infusion at a time when the bladder is very full and helping the patient's capability of retaining a large amount by the injection of opiates, preferably "Pantopon." The next problem is to accelerate the excretion of the radio-opaque substance as much as possible in order to have it at a maximum concentration in the renal pelvis and ureter at a certain point in time after the injection. Sodium iodide is advised as the radio-opaque substance and its excretion is accelerated by the simultaneous intravenous injection of urea. The latter substance has a strongly diuretic action and accelerates the excretion of the iodide.

Perineal Drainage After Suprapubic Prostatectomy.

A. FULLERTON (*British Journal of Urology*, March, 1929) describes an original method of inserting a rubber drain through the perineum after suprapubic prostatectomy has been performed. The tube affords dependent drainage of the bladder and the prostatic cavity while the patient is in the sitting or semi-recumbent position. Before the suprapubic operation is commenced an incision is made in the perineum parallel to the ischio-pubic ramus on one side and a little nearer the *tuber ischii* than the anus. The incision is about 3·75 centimetres (one and a half inches) long and its centre is on the line joining the ischial tuberosities. The knife simply cuts through skin and some of the ischio-rectal fat and then the index finger is made to burrow through the fat, passing behind and below to the base of the urogenital diaphragm until it passes to the medial side of the anterior edge of the *levator ani* muscle; here the postero-inferior portion of the prostatic capsule is touched. The suprapubic prostatectomy is carried out; one index finger is placed in the prostatic cavity and the other in the perineal wound, when an extremely thin septum between the two fingers is easily perforated by forceps. A 1·25 centimetre (half inch) diameter, moderately rigid tube is drawn up into the bladder, lateral holes in it drain the prostatic cavity as well. The author considers that sepsis is the most important problem as yet unsolved in the question of mortality after prostatectomy and holds that the lower mortality of perineal prostatectomy is largely due to the dependent drainage obtained. In the author's operation a suprapubic drain is used as well.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Women's Hospital, Melbourne, on July 17, 1929. The meeting took the form of a series of demonstrations by the members of the honorary staff.

Uterine Myomata.

DR. EDWARD R. WHITE presented a patient with a large submucous myoma. She was a *multipara*, aged forty-three years and complained of very free loss at her periods, with occasional floodings. On examination six weeks previously she had been very ill with profound secondary anæmia; a large smooth tumour had been found to arise from the pelvis to above the umbilicus. About 280 cubic centimetres (ten ounces) of blood had been transfused and three days later 568 cubic centimetres (twenty ounces) had also been given. At first the hæmoglobin value had been 30% and the red cell count 1,270,000. Three weeks later these had increased to 65% and 2,650,000. At the time of the meeting the blood examination revealed a hæmoglobin value of 85% and a red cell count of 4,200,000, and the patient looked very well.

Dr. White said that this patient well illustrated the conversion of a woman, extremely ill with secondary anæmia, into a good condition for operation by means of rest in bed, with general treatment and blood transfusions.

She had been operated upon two days later, when a large submucous myoma, affected by fatty degeneration, was removed by subtotal hysterectomy. The convalescence had been normal and she had left hospital on the eighteenth day.

The next patient was a young girl with multiple myomata. She had complained of profuse loss at the periods for years. On examination she had been anæmic, the uterus had been enlarged and several myomata were palpated. Dr. White said that in this patient the difficulty in choice of operation was well exemplified. Subtotal hysterectomy would have been quicker, easier and safer in an anæmic patient with several large myomata. But her youhtfulness had determined a myomectomy.

At operation six myomata had been excised and the bleeding controlled by temporarily clamping the ovarian vessels and by the use of Bonney's myomectomy clamp which was demonstrated. Already her periods were becoming more normal, both as regards duration and quantity lost. Her general condition had also much improved.

Endocrine Dysfunction.

Dr. White's third patient was a woman suffering from endocrine dysfunction with cervical stenosis and hæmatometra. She was aged thirty years and had five children, the youngest two years old.

Before marriage ten years previously the periods had been regular, but she had had only one period six years before. For the previous six months at monthly intervals she had had severe lower abdominal pain lasting three or four days, but for two weeks on the last occasion. On examination the thyreoid gland had not been palpable, though the result of the estimation of the basal metabolism was normal. The uterus had been felt to be slightly enlarged and rather softened; the tubes had been normal and the ovaries quite small.

At operation it had been found that the cervical canal was closed, but a sound had eventually been passed through some sticky adhesions and thirty cubic centimetres (one ounce) of dark fluid blood had escaped from the cavity of the uterus. On curettage the cavity had felt bare and no scrapings had been obtained. Dr. White said that the endometrium was usually atrophied in cases of hæmatometra. The amenorrhœa was not unusual in a woman with frequent pregnancies. After the last confinement the cervical canal had closed after some endocervicitis. Since then and while the patient was undergoing glandular therapy in the out-patient department, a partial but regular resumption of the menstrual bleeding had occurred, but the blood had been retained and given rise to the hæmatometra and the pain. A uterine sound passed at long intervals would keep the cervical canal patent.

The Use of Carbon Dioxide in Asphyxia Pallida.

DR. W. G. CUSCADEN showed an apparatus designed for the use of carbon dioxide in *asphyxia pallida*. An account of this will be published in a subsequent issue.

Retrodisplacement of the Uterus.

DR. ARTHUR SHERWIN discussed the question of the use of "Lipiodol" injections of the uterus and tubes in patients operated on for retrodisplacement of the uterus. He showed several patients and read their histories. He also demonstrated the skiagrams.

One patient had been subjected to extraperitoneal shortening of the round ligaments by the Alexander-Adams operation. A second patient had undergone intraabdominal shortening of the round ligaments by the Wylie-Mann operation, triple folding of the round ligaments by Baldy-Webster's technique. A third had undergone transplantation of the round ligaments into the abdominal wall by Gilliam's operation.

In a discussion on the question of the choice of operation it was agreed that whilst many factors had to be considered, yet when the uterus was freely movable and when there was no indication for surgical treatment of the appendix or pelvic organs, the Alexander-Adams operation was most advantageous to the patient. When the uterus was fixed or partly movable with or without accompanying indications for surgical treatment of adnexæ or appendix, opinions were divided between suitability of the Gilliam and the Wylie-Mann technique; the majority was in favour of the former. This was borne out by showing the hospital statistics for the previous year which proved the Gilliam operation to have been performed more than three times as frequently as any other suspending operation.

Dr. Sherwin also showed a patient who had been subjected to vagino-perineoplasty for contracted vaginal outlet. She was twenty-two years of age and had been married four months. She had never menstruated and had no adult development. The vaginal orifice was contracted and barely admitted a number 12 Hegar dilator; coitus was impossible. At operation two oblique vagino-perineal incisions had been made. They had been directed from within outwards in the lateral walls of the vagina and had extended downwards and outwards to the confines of the perineum. These incisions had been sutured with chromicized gut in the reverse direction and the resulting aperture readily admitted three fingers.

NOMINATIONS AND ELECTIONS.

THE undermentioned have been elected members of the Victorian Branch of the British Medical Association in Australia:

Milton, Gray Edison, M.B., Ch.B., 1929 (Univ. Melbourne), 37, John Street, Elwood, S.3.

Lalage, Rosamond Benham, M.B., Ch.B., 1929 (Univ. Melbourne), 25, Kenneally Street, Surrey Hills.

THE undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

Cook, Leslie James, M.B., B.S., 1928 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Dalgarno, Marjorie Clare, M.B., Ch.M., 1925 (Univ. Sydney), 44, South Parade, Campsie.

Manion, John Allan, M.B., Ch.M., 1926 (Univ. Sydney), 134, Boulevard, Dulwich Hill.

Smith, Frederick William, M.B., 1928 (Univ. Sydney), Gardener's Road, Rosebery.

Smith, Kenneth Stokes, M.B., Ch.M., 1926 (Univ. Sydney), 97, Darlinghurst Road, Darlinghurst.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A meeting of the Medical Sciences Club of South Australia was held at the University of Adelaide on July 5, 1929.

Serum Proteins.

Dr. Ray Hone raised a discussion on the serum proteins. He summarized the position as it had been during the time when he was actively working on the subject seven years previously and sought for information on some points raised in a previous discussion.

He drew attention to the following points, namely, that the serum increased from childhood to adult age; that the origin, according to Whipple, was in the liver. He cited the observations of D'Arcy Power on albuminuria in athletes (rowing crews) who had taken egg albumin. The results were very conflicting and it was the opinion of Dr. Hone that the idea of an albuminuria caused by the protein gaining access to the blood stream unaltered in any quantity was unphysiological and therefore improbable.

He then considered the various changes which blood proteins would confer upon that fluid, such as maintaining the viscosity, the protein being nutritive or being a tissue protein, blood being looked upon as a tissue. He referred to a suggestion made at a previous meeting that the protein of the blood had been looked upon as being one of the important carriers of carbon dioxide and stated that in his opinion this was incorrect. He, however, considered that the proteins did have some buffer value in the blood by virtue of the formation of sodium proteinate.

Whipple's theory that the proteins provided a necessary environment for the tissue cells was mentioned, together with that observer's work upon the gradual replacement of the protein by saline solutions.

The relation of the proteins to immunity was dealt with and it was considered that immunity was not related to the globulin content in a hard and fast manner. Methods of measurement of the protein content of the plasma were discussed, together with the points to be considered in the selection of cases, such, for example, as ascertaining the absence of other infections than the one under investigation. He cited patients of his own (nephritis) in whom there had been an albuminuria associated with unchanged blood protein, while there were others with low blood protein and no albuminuria. Van Slyke and Linder, using the vital red method, had disproved the contention of Reis that a low protein content indicated hydræmia.

The rise in serum globulin noted in many cases of infection, was not general. A rise in globulin might indicate an infection, but the indications were that in subacute infections there was no rise. Howell's observation was very significant, that new-born calves had scarcely any globulin in the serum, but after ingesting colostrum containing serum and globulin, manifested a rise in blood globulin content. This rise in blood globulin was *pari passu* with the transference of maternal immunity to the suckling. New-born infants' blood according to Lewis and Wills was low in globulin, but in Dr. Hone's patients this observation was not borne out.

Professor H. H. Woollard in answer to a question stated that the serum protein in the embryo began as an angioblastic production. He suggested that this might be the analogue of the process occurring throughout life.

Professor T. B. Robertson stated that the rise in globulin from toxin immunization was not proportional to the development of antitoxin and he stated that his attention had been originally drawn to the subject by a case in which there was a 90% globulin ratio occurring with enteric fever and gave an account of the development of his own work from that of Reis who had used whole serum and ascribed the changes found to dilution effects, changes which might be ascribed to variations in the proportions of the albumin and globulin.

Professor J. A. Prescott asked whether the method could be claimed to be more accurate than 5% on account of difficulties of protein separation.

Professor Robertson considered that it would not be more accurate than that, but he thought the nitrogen estimation, although more accurate, required too much blood for animal experiments. He further referred to the work of Galeotti who had treated the precipitation of protein by salts in terms of the phase rule which led to the conclusion that there was not more than one globulin. This contention, long since established by Galeotti, had been further supported by Dakin's work on racemization.

Dr. L. V. Bull referred to the work of Theobald Smith on the white scour in calves (due to intestinal infection). This condition occurred in calves separated from the mother and was prevented if the calf received colostrum owing to immunization.

THE MEDICAL BENEVOLENT ASSOCIATION OF NEW SOUTH WALES.

We have been requested to publish the following note by Dr. S. Littlejohn, the Honorary Treasurer of the Medical Benevolent Association of New South Wales.

All members of the profession in New South Wales should join the Medical Benevolent Association of New South Wales. It is surely the duty of all who can afford to do so, to subscribe the small sum of one guinea a year to help those who are less fortunate and are in need of help. Furthermore, the association is actually an insurance society which insures members who may meet with disaster from one cause or another, and their dependants against actual want. Further than this, it assists widows to earn a living and to support and educate their children. No one knows what the future may bring and let it be remembered that those members of the medical profession whose unfortunate dependants the association is supporting today, would have scouted a few years ago the idea of any such possibility.

The association is in urgent need of more funds and requires many more annual subscribers to enable it to carry on its benevolent functions. Intending members should apply to the Honorary Secretary, The Medical Benevolent Association of New South Wales, 21, Elizabeth Street, Sydney. All subscriptions will be most gratefully acknowledged.

University Intelligence.

THE UNIVERSITY OF SYDNEY.

A meeting of the Senate of the University of Sydney was held on November 4, 1929.

The following degrees were conferred *in absentia*:

Doctor of Medicine (M.D.): Joseph Lexden Shellshear, Cecil Evelyn Cook.

Master of Surgery (Ch.M.): Clara Murray Wilson (formerly Clara Murray Sams).

The Graziers' Association of New South Wales advised that it had arranged for the provision of a refrigerator and the sum of £75 for the purchase of sheep and animal food to enable Mr. H. R. Carne, B.V.Sc., to continue his researches in connexion with caseous lymphadenitis at the School of Veterinary Science. The gifts were received with grateful thanks.

Professor E. G. Waterhouse and Mr. A. H. Robinson, M.A., were appointed as representatives of the Senate on the Board of Directors of the University Union for the year 1929-1930.

Miss E. M. Mallarky, M.A., and Miss E. M. Hindmarsh, B.Sc., were apopinted to represent the Senate on the Board of Directors of the Women's Union for the year 1929-1930.

The appointment of the following examiners was approved:

Third Degree Examination in Anatomy: Dr. H. R. G. Poate and Dr. F. A. Maguire.

Therapeutics and *Materia Medica*: Dr. M. Lidwill.

Pathology: Dr. J. E. V. Barling.

Veterinary Anatomy: Dr. C. J. M. Walters, B.V.Sc.

Veterinary Surgery and Obstetrics: Mr. V. E. H. Davis, B.V.Sc.

Veterinary Medicine: Mr. J. R. Stewart, B.V.Sc.

Veterinary Pathology and Bacteriology: Dr. H. R. Seddon.

Zootechny: Lieutenant-Colonel Max Henry, D.S.O., B.V.Sc.

Obituary.

THOMAS JENNER VERRALL.

It is with great regret that we have to announce the death on October 4, 1929, of Sir Thomas Jenner Verrall. Although he retired from practice some time ago, he had continued to work for the benefit of the medical profession almost to the end of his life.

Thomas Jenner Verrall was born in 1852. He was educated at Marlborough and later became a medical student at Saint Bartholomew's Hospital, London, at a time when James Paget and Luther Holden were in their prime. In 1876 he obtained the diplomas of member of the Royal College of Surgeons of England and licentiate of the Royal College of Physicians of London. He practised at Brighton for many years and attained a considerable degree of eminence. He was a very sound diagnostician, a competent and reliable practitioner and a most sympathetic and wise counsellor.

In 1895 after having manifested his interest in the affairs of the medical profession in Brighton he was appointed a member of the Council of the British Medical Association. He was consistent in his attendance at meetings and proved himself a valuable councillor and a hard worker. A few years later, when the British Medical Association was reconstituted, he was a member of the first new council. He was also appointed a representative of his Branch. From that time (1901) onward he took a prominent part in the affairs of the British Medical Association. Ten years later he was appointed Chairman of the Representative Body, a position he held for five years. At the outbreak of war he was chosen to be Chairman of the Central Medical War Committee and in this capacity he achieved a great deal and performed much valuable work for the country and Empire. In 1916 at the Representative Meeting he supported J. A. Macdonald in paying a deep tribute to the late Victor Horsley who had died in Mesopotamia. At that meeting Dr. E. B. Turner was in the chair. In 1919 in recognition of his services to the Empire he received the honour of knighthood. He was given an honorary degree of LL.D. by the University of Aberdeen. Since 1922 Thomas Jenner Verrall has acted as representative of various Branches of the British Medical Association in Australia on the Council of the Association. His name has thus become very familiar to many Australian practitioners who did not have the privilege and advantage of a personal acquaintance with him.

He was a man of much strength of character, of culture and refinement. He had a remarkably clear mind and was a forceful speaker. He was a man of the highest integrity. The charm of his personality, his dignified bearing and his transparent good nature endeared him to all with whom he came in contact. His popularity was the result of his sterling qualities. He neither sought it nor did he use any devices to secure it. The world would be a better place if there were more true gentlemen of the type of Thomas Jenner Verrall.

Correspondence.

THE BICOLOURED GUAIAC TEST IN CEREBRO-SPINAL FLUID.

Sir: Doubtless many of your readers would use the gold-sol test for indicating the various general paralytic, luetic or meningeal colloidal curves in the spinal fluid were not its manufacture so uncertain and suitable triple distilled water so difficult to obtain. The colloidal paraffin substitute, while easier to make and quite permanent, is not so sensitive in reaction or results. We are indebted to Dr. Finckh for bringing to our notice the one tube takata-ara colloidal reaction in your issue of June 22, 1929, page 852. We have found this test most reliable and easy of manufacture.

Nevertheless many practitioners and pathologists may prefer a ten tube test providing the well known colloidal curves.

The claims of Dr. de Thurso in *Brain* (July, 1929, Volume LII, Part II), that his bicoloured guaiac test utilizes permanent reagents, has clear cut reactions and is even more sensitive than the gold-sol test, appears to us quite justified in the few scores of tests we have done. He likewise maintains that he believes he has evidence that an apparently clinically healthy, but serologically positive syphilitic who gives a general paralytic curve in his spinal fluid, will become a general paralytic within three years and therefore should undergo malarial treatment at once without waiting for the clinical signs.

The reagents are easily obtained if one recognizes that brilliant fuchsin which may not be found in one's stock is really diamant fuchsin of the old German drug houses and these brands seem to act as well as Gurr's, of London, whose stains he recommends.

The reagents:

(i) British Pharmacopœia tincture of guaiacum resin, 20% in alcohol; a good sample freshly made up can be got from any chemist.

(ii) Brilliant (diamant) fuchsin, 0·5% in absolute alcohol.

(iii) Naphthol green, 0·5% in distilled water.

(iv) 10% sodium chloride from which we make the 0·2% saline used in the spinal fluid dilution.

(v) A 0·5% solution of anhydrous sodium carbonate.

Keep all in dark glass stoppered bottles in a cool place.

Preparing the colloidal solution:

Place 40 cubic centimetres of distilled water in a small Erlenmeyer flask, then pour in slowly down side of flask with pipette, 0·22 cubic centimetre of guaiac tincture in nine cubic centimetres of absolute alcohol (9·22 cubic centimetres added) lightly and continuously shaking the flask. The suspension should be yellowish-white, transparent and only feebly opaque to overhead light. Still agitating slowly in a circular manner add two cubic centimetres of naphthol green solution. As soon as the mixing is completed add 0·3 cubic centimetre of the diamant fuchsin solution. The result should be a cherry red, transparent, slightly opaque mixture to overhead light. Some samples appear purplish to direct light, but seem to act. After twenty minutes it is ready for use.

The test: The usual series of dilutions are made in ten small tubes. With a pipette half a cubic centimetre of spinal fluid is placed in the first two tubes. Then starting from the second tube we add to each tube half a cubic centimetre of 0·2% saline, containing one cubic centimetre of 0·5% sodium carbonate to each 100 cubic centimetres of saline. The saline mixture should be made fresh from the strong saline solution. Beginning from the second tube we transfer half a cubic centimetre to the third and after mixing half a cubic centimetre to the fourth and so on, as is usual with the gold method. To each tube we then add half a cubic centimetre of the colloidal suspension. Gently shake each tube.

Results: No change, 0, the solution remains unchanged, red, without precipitate; 1, a light red colour with slight precipitate; 2, greyish-red colour with evident sedimentation; 3, greyish-green colour, red precipitate; 4, vivid green colour with red precipitate in bottom of tube. Read after twenty to twenty-four hours. A typical paretic curve would therefore read 4, 4, 4, 3, 3, 2, 1, 0, 0, 0, as in the gold sol test. The contrast is certainly striking.

Yours, etc.,

OLIVER LATHAM.

Mental Hospitals Laboratory,
New South Wales.
October 27, 1929.

THE TONSILS AND THE UVULA.

Sir: What is the uvula for? I have been informed that it is to keep the tonsils apart. In view of the fact that the profession has discovered that the tonsils are mainly for removal and that in the majority of cases had been or were being removed as a major operation, it has now become necessary to consider the enucleation or should we not call it the evulsion of the uvula.

Any period from ten days to a fortnight in an expensive hospital would be necessary for the complete recovery of the patient and that under no circumstances should the operation be performed under any simple method of anæsthesia, but that a pantechnicon is necessary to carry the operative and anæsthetic apparatus from point to point.

Perhaps some of my brother professional men may be able to enlighten me upon the above.

For how much longer are we and the public to put up with this operative farce as regards tonsillectomy as a major operation? Why not circumcision? It is quite as necessary at times. In the big majority of cases the tonsils can be completely and effectively removed by the simple blunt guillotine method in the hands of an operator who knows his work.

We are today seeing patients placed on the operation table and subjected to the slow torture of dissection under a prolonged and quite unnecessarily protracted stage of anæsthesia, with the not lessened, but the increased risk of post-operative hæmorrhage.

If the profession as a whole and the public could only get a real glimpse of the work that has gone on in the past few years in regard to tonsillectomies, they would be disgusted and call a halt and demand the simpler methods.

Yours, etc.,

R. W. Hornabrook.

Melbourne.
October 21, 1929.

ENDOMETRIOMATA.

Sir: In the current number of The Medical Journal of Australia you have been good enough to publish my report of a case of endometriosis and in another part of the journal to comment both upon this report and upon the paper on the subject that I read at the recent congress.

May I point out that my suggestion that in cases of endometriosis it may be advisable to ligate or excise the Fallopian tubes was made with the object of eliciting an expression of opinion from my gynæcological colleagues and not as a declaration of policy?

I have no personal experience of such a prophylactic measure and the suggestion was made on theoretical grounds which imply an acceptance of Sampson's view of the ætiology of endometriosis.

Yours, etc.,

Bernard Dawson.

8, King William Street,
Adelaide.
November 11, 1929.

A QUOTATION FROM SHAKESPEARE.

Sir: In his entertaining article, "Olla-Podrida," Dr. W. J. L. Duncan quotes from Shakespeare:

> This distemper'd messenger of wet,
> The many-colour'd Iris, rounds thine eye?

The poet's reference is not, however, as Dr. Duncan thinks, to the iris of the eye-ball, but to the dark rings that appear under the eyes in states of bad health or depression of spirits. It is these that are the signs of bad weather ("distemper'd"), the heralds of a rain of tears. The correctness of this explanation may be shown by a quotation from "The Rape of Lucrece":

> And round about her tear-distained eye,
> Blue circles stream'd, like rainbows in the sky.

Yours, etc.,

Eric Jeffrey.

4, Douglas Avenue,
Lower Sandy Bay,
Tasmania.
November 15, 1929.

Proceedings of the Australian Medical Boards.

NEW SOUTH WALES.

The undermentioned have been registered under the provisions of *The Medical Act*, 1912 *and* 1915, of New South Wales, as duly qualified medical practitioners:

Baylis, Edna Isabel, M.B., B.S., 1929 (Univ. Sydney).
Cooper, Bryce Arnot, M.B., B.S., 1929 (Univ. Sydney).
Courtney, Geoffrey Charles Palliser, M.B., B.S., 1925 (Univ. Melbourne), 30, Botany Street, Randwick.
Douglas, Stephen, L.M.S.S.A. (London), 1925, 13, Waverley Street, Waverley.
Grant, Alan Mostyn Bradford, M.B., B.S., 1929 (Univ. Sydney).
Kennedy, Richard Thomas, M.B., B.S., 1929 (Univ. Sydney).
King, William Stevenson, M.B., Ch.B., 1916, D.P.H., 1921 (Univ. Saint Andrews), c.o. Australian Bank of Commerce, Randwick.
Lawrance, Kenneth George, M.B., 1929 (Univ. Sydney).
Lovell, Stanley Hains, M.B., B.S., 1929 (Univ. Sydney).
Stephens, Henry James Bondfield, M.B., B.S., 1929 (Univ. Melbourne), c.o. A.M.P. Society, Cobargo.
Taylor, Clive William, M.B., B.S., 1929 (Univ. Sydney).

For additional registration:

Buckingham, Reginald Eric, F.R.C.S. (Edinburgh), 1929.
Miller, Ian Douglas, F.R.C.S. (England), 1928.

Change of name:

Farran-Ridge, Thornleigh, to Farranridge, Tom.
Smith, Frederick William, to Smith, Frederick Wilkie (Gardener's Road, Rosebery).

VICTORIA.

The undermentioned has been registered under the provisions of Part I of the *Medical Act of* 1915, of Victoria, as a duly qualified medical practitioner:

Cumming, Robert, M.B., Ch.B., 1898 (Univ. Edinburgh), Lancefield.

HALFORD ORATION.

The annual Halford Oration was delivered on November 26, 1929, in the Albert Hall, Canberra, by Professor D. Welsh, M.D., D.Sc., F.R.C.P., Dean of the Faculty of Medicine of the University of Sydney, who dealt with the life history of cancer. The oration was founded in connexion with the Institute of Anatomy by the members of the family of the late Professor Halford who occupied the chairs of anatomy, physiology and pathology at the Melbourne University and was the founder of the first medical school in the southern hemisphere. The inaugural oration was delivered last year by Professor Osborne who dealt with the life and works of Professor Halford.

Books Received.

DEVILS, DRUGS AND DOCTORS: THE STORY OF THE SCIENCE OF HEALING FROM MEDICINE-MAN TO DOCTOR, by Howard W. Haggard, M.D.; 1929. London: William Heinemann (Medical Books) Limited. Royal 8vo., pp. 427, with illustrations. Price: 21s. net.

AIDS TO DERMATOLOGY AND VENEREAL DISEASE, by R. M. B. Mackenna, M.A.; M.B., B.Ch., M.R.C.P., M.R.C.S.; 1929. London: Baillière, Tindall and Cox. Foolscap 8vo., pp. 236. Price: 3s. 6d. net.

MINOR SURGERY, by Frederick Christopher, M.D., F.A.C.S., with a foreword by Allen B. Kanavel, M.D., F.A.C.S.; 1929. Philadelphia and London: W. B. Saunders & Co. Melbourne: James Little. Royal 8vo., pp. 694, with illustrations. Price: 37s. 6d. net.

THE NOSE, THROAT AND EAR AND THEIR DISEASES, Edited by Chevalier Jackson, M.D., Sc.D., LL.D., F.A.C.S., and George Morrison Coates, A.B., M.D., F.A.C.S.; 1929. Philadelphia and London: W. B. Saunders & Co. Melbourne: James Little. Royal 8vo., pp. 1177, with illustrations. Price: 63s. net.

THE DIABETIC A B C, by R. D. Lawrence, M.A., M.D., M.R.C.P. (London); 1929. London: H. K. Lewis & Co., Ltd. Demy 8vo., pp. 55. Price: 3s. 6d. net.

SURGICAL PATHOLOGY, by William Boyd, M.D., M.R.C.P. (Edin.), Dipl. Psych., F.R.S. (Cantab.); 1929. Philadelphia and London: W. B. Saunders Company; Melbourne: James Little. Royal 8vo., pp. 933, with illustrations. Price: 55s. net.

VARICOSE VEINS, by T. Henry Treves-Barber, M.D., B.Sc., with Foreword by H. W. Carson, F.R.C.S.; 1929. Bristol: John Wright & Sons Limited. Crown 8vo., pp. 120, with illustrations. Price: 6s. net.

Diary for the Month.

DEC. 3.—Tasmanian Branch: Council.
DEC. 3.—New South Wales Branch, B.M.A.: Ethics Committee.
DEC. 4.—Victorian Branch, B.M.A.: Annual Meeting; Council.
DEC. 4.—Western Australian Branch, B.M.A.: Council.
DEC. 5.—New South Wales Branch, B.M.A.: Branch.
DEC. 5.—Tasmanian Branch, B.M.A.: Council.
DEC. 6.—Queensland Branch, B.M.A.: Council.
DEC. 10.—Tasmanian Branch, B.M.A.: Branch.
DEC. 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
DEC. 10.—New South Wales Branch, B.M.A.: Organization and Science Committee.
DEC. 11.—Central Northern Medical Association, New South Wales.
DEC. 11.—South Sydney Medical Association, New South Wales.
DEC. 12.—Victorian Branch, B.M.A.: Branch (Annual).
DEC. 12.—Victorian Branch B.M.A.: Council.
DEC. 12.—Section of Orthopædics, New South Wales Branch, B.M.A.
DEC. 13.—Queensland Branch, B.M.A.: Branch (Annual).
DEC. 17.—Tasmanian Branch, B.M.A.: Council.
DEC. 17.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xviii.

CAIRNS HOSPITAL BOARD, QUEENSLAND: Resident Medical Officer.

DIRECTOR-GENERAL OF PUBLIC HEALTH, SYDNEY, NEW SOUTH WALES: Honorary Medical Officers.

LAUNCESTON PUBLIC HOSPITAL, TASMANIA: Junior Resident Medical Officer (male).

THE BRISBANE AND SOUTH COAST HOSPITALS BOARD: Honorary Vacancies.

THE attention of our readers is directed to an announcement in the advertising pages of this issue that the position of Medical Superintendent of the Alfred Hospital, Prahran, is vacant and that the board of the hospital is inviting medical practitioners to apply for the position.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 21, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company, Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Members accepting appointments as medical officers of country hospitals in Queensland are advised to submit a copy of their agreement to the Council before signing. Brisbane United Friendly Society Institute. Mount Isa Hospital.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Contract Practice Appointments in South Australia. Booleroo Centre Medical Club.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Medical practitioners are requested not to apply for appointments to positions at the Hobart General Hospital, Tasmania, without first having communicated with the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales.

Editorial Notices.

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